A Non-Targeted Metabolomics Approach to Metabolite Analysis in a Complex Matrix Using a Sensitive High-Speed Mass Spectrometer

ThPC091

ABSTRACT

Detection of metabolites in a complex sample poses analytical challenges due to the potential for large numbers of endogenous components to interfere with the detection and to express variable sensitivity of relevant metabolites. In this study, nontargeted metabolite detection was performed by using a combination of nontargeted methods created using LightSight 1.5 software. The LC/MS profile of reactive intermediate and drug metabolites is shown in Figure 9. LC/MS Profile of Reactive Intermediate and Drug Metabolites is shown in Figure 9.

INTRODUCTION

Metabolite detection by LC/MS is an essential technique used to identify the identity and purity of metabolites. Metabolites that are present in biological samples are often a chemical mixture of low abundance and diverse structure, which makes their detection challenging. Mass spectrometry (MS) is widely used for the detection of metabolites due to its high sensitivity and specificity. The MS/MS analysis allows for the identification of metabolites by comparing the fragmentation pattern of the sample with the fragmentation pattern of known reference compounds.

RESULTS

Figure 1. MRM method as Survey Scan in Analyst® 1.5 software

Figure 2. Pharmacokinetic Profile of Carbamazepine in Vivo Rat Plasma

Figure 3. LC/MS Profile of Reactive Intermediate and Drug Metabolites

Figure 4. EA Trace Extractor XIC

Figure 5. XIC of +MRM (451 pairs): Exp 1, 208.1/208.1 Da ID: 208... Max. 2.3e5 cps.

Figure 6. Potential Metabolites with Similar MS/MS spectrum on Parent

Figure 7. Potential Metabolites with Similar MS/MS spectrum on Parent

Figure 8. Chromatograms (XIC's) of precursors that gave rise to a high-level peak, with very good quality, diagnostic MS/MS fragmentations. These precursors were found at different RT's and were present in all samples. The high speed and sensitivity of the QTRAP® 5500 was used for this analysis. Non-targeted methods were created using 1) Q3 and 2) MIM as survey scan in two separate methods. Product ion scans were automatically collected on Q3 mode from the survey scans. In the positive ion mode, MSMS spectra of +Q3 (enhanced resolution) were monitored, and the method used was: MRM-Q3-Q3. The MRM scan, resulting in the parent ions (210 Da → 192 Da) was conducted following the MRM 5500 scan in the positive ion mode. The MRM scan was then followed by a survey scan of the same parent ion. The survey scan was then followed by a MSMS scan of the selected parent ion. The survey scan was then repeated, and the MSMS scan was then repeated, and the process was repeated until the end of the chromatogram.

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