

IDENTIFICATION OF METABOLITES IN PLASMA AND URINE USING CAPILARY LC COUPLED TO A HYBRID ORTHOGONAL TIME OF FLIGHT MASS SPECTROMETER EQUIPPED WITH NANOLOCKSPRAY

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Tandem quadrupole and Time Of Flight mass spectrometry is now widely used to generate DMPK information for new compounds easily and in a relatively fast manner. One other important area in the drug discovery and development process is the identification of drug metabolites in both *in vitro* and *in vivo* samples. Plasma metabolites are often difficult to detect by typical screening methods due to their low levels in circulation. Therefore, the aim of this work was to develop a method utilizing the capabilities of both CAPLC and TOF detection coupled with NanoLockspray for identification of circulatory metabolites. Plasma samples were analysed using different time points. The samples were ran using a dual spray nano-LC interface with which analyte was introduced into one spray and a reference compound was introduced into the other spray. The data from the reference spray is acquired independently of the analyte spray and is used to lock-mass correct the analyte data to provide exact mass results. A capillary LC system was also used but the flow taken through a splitter and the column used was a 180 μ m x 150 mm, C18. Moreover, further experiments were carried out using MS/MS and Neutral Loss acquisitions using the dual spray nano LC interface. As a result, we were able to accurately measure all of the identified metabolites to within 5ppm RMS. The added advantage of using nano-scale chromatography was the increased level of sensitivity gained by using this particular approach in comparison with analytical flow rates. Moreover, sample consumption was also reduced allowing an increased number of experiments to be carried out from limited resources.
