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Pragmatic and rapid analysis of carbonyl, oxidation and chlorination nucleoside-adducts in murine tissue by UPLC-ESI-MS/MS

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Abstract

Nucleoside-adduct analysis by liquid chromatography mass spectrometry is a powerful tool in genotoxicity studies. Efforts to date have quantified an impressive array of DNA damage products, although methodological diversity suggests quantification is still a challenging task. For example, inadequate co-examination of normal nucleosides, cumbersome sample preparation and large DNA requirements were identified to be recurring issues. A six-minute ultra-performance liquid chromatography method is presented which adequately separates seven candidate nucleoside-adducts from the four unmodified nucleosides. The method was sensitive to 1 adduct per 10^8 normal bases with 20 µg DNA input for most targets. The method was shown to be accurate (81 – 119% across quintuplets of six tissue types) and precise (relative standard deviation 4 – 13%). The fast method time facilitated a second quantitation for normal nucleosides at an appropriate dilution, allowing DNA damage concentrations to be contextualised accurately sample-to-sample. From DNA samples, the analytical processing time was <8 hours, and 96 samples can easily be prepared in a day. The method was used to quantify carbonyl, chloro- and oxo- adducts in murine tissue samples.