Quantitative profiling of prostaglandins as oxidative stress biomarkers in vitro and in vivo by negative ion online solid phase extraction - Liquid chromatography-tandem mass spectrometry

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Free radical-mediated oxidation of arachidonic acid to prostanoids has been implicated in a variety of pathophysiological conditions such as oxidative stress. Here, we report on the development of a liquid chromatography-mass spectrometry method to measure several classes of prostaglandin derivatives based on regioisomer-specific mass transitions down to levels of 20 pg/ml applied to the measurement of prostaglandin biomarkers in primary hepatocytes. The quantitative profiling of prostaglandin derivatives in rat and human hepatocytes revealed the increase of several isomers on stress response. In addition to the well-established markers for oxidative stress such as 8-iso-prostaglandin F2α and the prostaglandin isomers PE2 and PD2, this method revealed a significant increase of 15R-prostaglandin D2 from 236.1 ś 138.0 pg/1E6 cells in untreated rat hepatocytes to 2001 ś 577.1 pg/1E6 cells on treatment with ferric NTA (an Fe(3+) chelate with nitrilotriacetic acid causing oxidative stress in vitro as well as in vivo). Like 15R-prostaglandin D2, an unassigned isomer that revealed a more significant increase than commonly analyzed prostaglandin derivatives was identified. Mass spectrometric detection on a high-resolution instrument enabled high-quality quantitative analysis of analytes in plasma levels from rat experiments, where increased concentrations up to 23-fold change treatment with Fe(III)NTA were observed.

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