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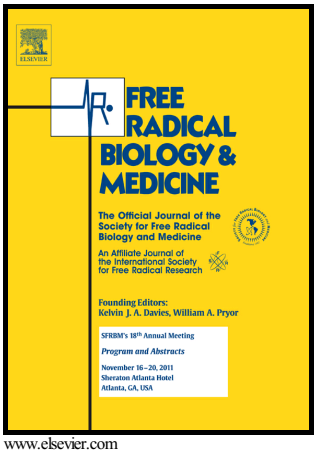

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Analysis of Eicosanoid Oxidation Products in Alzheimer Brain by LC-MS with Uniformly 13C-Labeled Internal Standards

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Abstract

The quantitative analysis of polyunsaturated fatty acyl (PUFA) chain oxidation products in tissue samples by mass spectrometry is hindered by the lack of durable internal standards for the large number of possible products. To address this problem in a study of oxidative PUFA degradation in Alzheimer's disease (AD) brain, uniformly ^{13}C-labeled arachidonic acid (ARA) was produced biosynthetically, and allowed to oxidize under controlled conditions into a mixture of U-^{13}C-labeled ARA oxidation products. The components of this mixture were characterized with respect to their partitioning behavior during lipid extraction, their durability during saponification, trends in mouse brain tissue concentrations during post mortem intervals, and their overall suitability as internal standards for multiple-reaction monitoring tandem mass spectrometry. This mixture has now been used as a set of internal standards to determine the relative abundance of ARA and 54 non-stereospecific oxidation products in milligram samples of brain tissue. Many of these oxidation products were recovered from both healthy mouse and healthy human brain, although some of them were unique to each source, and some have not heretofore been described. The list of oxidation products detected in AD brain tissue was the same as in healthy human brain, although simple hydroxy-eicosanoids were significantly increased in AD brain. while more complex oxidation products were not. These results are consistent with an increased level of chemically-mediated oxidative ARA degradation in Alzheimer's disease. However, they also point to the existence of processes that selectively produce or eliminate specific oxidation products, and those processes may account for some of the inconsistencies in previously reported results.

Graphical abstract