

"Not just fat" – Exploring Octadecanoids as Novel Bioactive Lipids in Inflammation



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Oxylipins are oxygenated compounds that are formed from fatty acids by reaction(s) involving at least one step of mono- or dioxygenase-catalyzed oxygenation as well as products of auto-oxidation. The most studied class of oxylipins are eicosanoids, which are derived from the 20-carbon polyunsaturated fatty acid (PUFA) arachidonic acid via cyclooxygenase (COX), lipoxygenase (LOX) and cytochrome P450 (CYP) activity. However, 18-carbon fatty acids including oleic, linoleic, alpha-linolenic, and gamma-linolenic acid can also be metabolized by these same enzymes, resulting in a complex combination of structurally heterogeneous 18-carbon oxylipins, collectively defined as octadecanoids. These compounds are derived from the diet and constitute our primary dietary source of fat. Research into the bioactivity of octadecanoid lipid mediators is increasing, with studies showing their involvement in multiple disease processes including pain modulation and thermogenesis, as well as regulation of inflammation and immune function. Causative roles in the etiology of respiratory diseases have been reported in asthma, COPD and acute respiratory distress syndrome (ARDS). A major impediment to the study of octadecanoids is a lack of dedicated analytical methods for their quantification, with most studies to date focusing on a few compounds for which analytical standards are available. We developed an integrated analytical workflow combining chiral separation by supercritical fluid chromatography (SFC) and reversed-phase liquid chromatography (LC) coupled to tandem-MS detection for quantification of a broad panel of octadecanoids. The platform includes >100 custom-synthesized analytical and internal standards to extend the coverage of the octadecanoid synthetic pathways. A total of 173 octadecanoids could be separated by chiral SFC and complex enantioseparations could be performed in <13 minutes, while the achiral LC method separated 97 species in 13.5 minutes. This talk will provide examples of the analysis of octadecanoids demonstrating their role in multiple respiratory diseases including asthma and COPD as well as a recent clinical trial in which COVID-19 patients were treated with intravenous omega-3 fatty acids. The findings will collectively highlight the importance of octadecanoids in disease etiology, demonstrating that these dietary fat-derived compounds are potent bioactive lipid mediators.

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