Inhibition of Inflammatory Responses by Biotransformation Products of Polyunsaturated Fatty Acids (PUFA) and Structural Characterization of Active Compounds by LC-MS/MS

Petta, T;[1] Secatto, A;[2] Faccioli,LH;[2] Souza,GHMF;[3] Labate,CA;[4] Moraes, LAB[1]

1 University of São Paulo,FFCLRP, Ribeirão Preto/ BR

[2] University of São Paulo, FCFRP, Ribeirão Preto/BR

[3] Mass Spectrometry Applications Research and Development Laboratory, Waters Corporation,Barueri/BR

[4] University of São Paulo, ESALQ ,Ribeirão Preto/BR

The aim of this work was to produce new models of oxylipids with anti-inflammatory potential analogs in structure to lipid mediators (resolvins, lipoxins, protectins) employing fungal biotransformation of polyunsaturated fatty acids (PUFA). For this purpose, linolenic acid (ALA), linolenic acid (LNA) and ricinoleic acid (RC) were the biotransformation substrates for the fungi *Aspergillus niger*. We investigated the capacity of the biotransformation crude extracts and chromatographic fractions obtained by HPLC preparative to inhibit inflammatory responses through quantification of nitric oxide (NO) and tumor necrosis factor (TNF-α) in macrophages RAW-267.4 stimulated with LPS. The most active compounds were characterized by LC-MS/MS as the regioisomers 9-KOTE (9-keto-10E,12Z,15Z-octadecatrienoic acid) and 13-KOTE (13-keto-9Z,11E,15Z-octadecatrienoic acid). Analysis were performed employing an Acquity UPLC (Waters) coupled to a Xevo TQ-S mass spectrometer (Waters). Additionally to LC-MS, we developed a methodology to separate regioisomeric oxylipids, based on IM-MS (Ion Mobility-Mass Spectrometry). The standards 9-HODE (9-hydroxy-10E,12Z,15Z-octadecatrienoic acid) and 13-HODE (13-hydroxy-9Z,11E,15Z-octadecatrienoic acid) were separated in a Synapt and Synapt G2 (Waters). The relevance of this work was to show that biotransformation is a powerful strategy to be employed for the production of new molecular models to be applied in the treatment of inflammatory diseases.