Development of an On-Line Liquid Chromatography-Electrospray Tandem Mass Spectrometry Assay to Quantitatively Determine Aldehydes Derived fron Lipid Peroxidation in ALS Animal Models

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Aldehydes, endogenous toxic metabolites of lipid peroxidation, have been implicated in pathogenesis of numerous diseases, such as Amyotrophic Lateral Sclerosis (ALS). This neurodegenerative disease results from death of motor neurons, culminating in progressive muscle paralysis. Mutants forms of cooper/zinc superoxide dismutase (SOD1) have been identified in a subset of individuals with familial ALS. Transgenic rats carrying the $SOD1^{G93A}$ develops a neuron-killing disease that resembles the human condition. Some studies showed that DNA and proteins lesions can be formed from reaction with aldehydes formed during lipid peroxidation. However, few studies evaluate the identity of this aldehydes. We developed a HPLC copled mass spectrometry method to quantify aldehydes produced in brain and spinal cord of ALS animal models. The method relies in the analysis of 2,4-dinitrophenylhidrazones derivatization products with the following aldehydes: 4-hidroxy-2-nonenal (HNE), 2,4-decadienal, 2,4-nonadienal, 2,4-heptadienal, 2,4-hexadienal and 2-hexenal. This very sensible and reprodutible methodology detect 1 pmol of aldehyde per mg of brain and spinal cord. Our results showed that all aldehydes with exception of HNE are present in similar amounts in the sample. This could reflect HNE high reactivity towards biomolecules. With this new methodology we expect to identify and quantify a possible aldehyde candidate that could be used as a biomarker for this disease.

Keywords: aldehydes, lipid peroxidation, HPLC-MS/MS, ALS.

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