Investigation of the Detoxification Mechanism of Unsaturated Aldehydes in Tissues from Transgenic Rat Model of Amyotrophic Lateral Sclerosis

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The lipid peroxidation reaction generates, as secondary products, \(\alpha,\beta\) – unsaturated aldehydes. These aldehydes act as bifunctional electrophiles that can covalently modify fatty acid, DNA, and proteins. Current evidences suggest the involvement of these aldehydes in the pathogenesis of several disorders, such as inflammatory, metal storage, neurodegenerative diseases, and cancer. The detoxification mechanisms of these aldehydes is through conjugation with glutathione (GSH) in cytosol or, alternatively by conjugation with other endogenous peptides. The L- carnosine (CAR) and related peptides (CAR-P) are dipeptides widely found in skeletal muscle and central nervous system, which recent works indicate that these peptides actively participates in the elimination of 4-hydroxy-2-nonenal (HNE) in cell. Thus, the aim of this work is to investigate the formation of carnosine adducts with HNE and acrolein (ACR) in muscle, nervous system, plasma and urine of transgenic rat model of SOD\(^{G93A}\) mutant-mediated amyotrophic lateral sclerosis (ALS). Stable adducts were prepared \textit{in vitro}, isolated by reverse-phase HPLC and characterized by mass spectrometry. A method involving on-line HPLC with electrospray tandem mass spectrometry detection has been developed for the analysis of CAR-ACR and CAR-HNE in rat tissues. Preliminary results showed that this newly developed methodology enabled us to detect adducts with \(m/z\) 305 \(\rightarrow\) 231 (CAR-ACR) and \(m/z\) 383 \(\rightarrow\) 266 (CAR-HNE) in skeletal muscle from both control and ALS SOD\(^{G93A}\) rats. The analysis of these products in tissues of transgenic rat model for ALS may indicate possible biomarkers of ALS.

Word Keys: Carnosine, aldehyde \(\alpha,\beta\) – unsaturated, ALS

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