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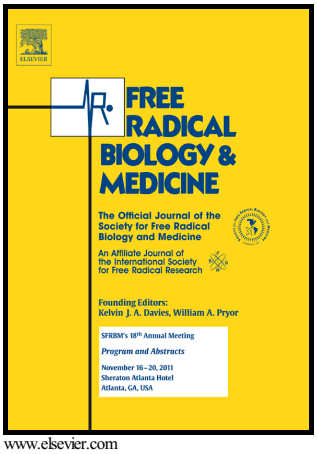

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Ergothioneine products derived by superoxide oxidation in endothelial cells exposed to high-glucose

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Abstract

Ergothioneine (Egt), 2-mercapto-L-histidine betaine (ESH), is a dietary component acting as antioxidant and cytoprotectant. *In vitro* studies demonstrated that Egt, a powerful scavenger of hydroxyl radicals, superoxide anion, hypochlorous acid and peroxynitrite, protects vascular function against oxidative damages, thus preventing endothelial dysfunction. In order to delve the peculiar oxidative behavior of Egt, firstly identified in cell free-systems, experiments were designed to identify the Egt oxidation products when endothelial cells (EC) benefit of its protection against high-glucose (hGluc). HPLC-ESI-MS/MS analyses revealed a decrease in the intracellular GSH levels and an increase in the ophthalmic acid (OPH) levels during hGluc treatment. Interestingly, in the presence of Egt, the decrease of the GSH levels was lower than in cells treated with hGluc alone, and this effect was paralleled by lower OPH levels. Egt was also effective in reducing the cytotoxicity of H_2O_2 and paraquat (PQT), an inducer of superoxide anion production, showing a similar time-dependent pattern of GSH and OPH levels, although with peaks occurring at different times. Importantly, Egt oxidation generated not only hercynine (EH) but also the sulfonic acid derivative (ESO_3H) whose amounts were dependent on the oxidative stress employed. Furthermore, *cell-free* experiments confirmed the formation of both EH and ESO_3H when Egt was reacted with superoxide anion. In summary, these data, by identifying the EH and ESO_3H formation in EC