NEUROPROTECTIVE EFFECTS OF SIMPLE ORGANOSELENO COMPOUNDS

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Overproductions of reactive oxygen and nitrogen species are involved in the process of either installation and/or progression of neuropathological coditions, including brain ischemia, Parkinson and orofacial dyskinesia. Unfortunately there is no effective treatment for counteracting them. Consequently the research and the development of new compounds with antioxidant activity are highly desirable. In the last three decades, a variety of organochalcogenides with antioxidant properties have been synthesized in different laboratories. Ebselen and diphenyl diselenide $(PhSe)_2$ have been used in a variety of in vitro and in vivo models of neurotoxicity. Of particular importance, Ebselen was used 10 years ago in 3 clinical trials with relative success in brain pathologies associated with ROS overproduction. The neuroprotective mechanism(s) of organochalcogenides seem(s) to involve their glutathione peroxidase/thioredoxine reductase like activity. Thus, in the presence of reducing thiols, they decompose H_2O_2 and ROOH. In addition, chalcogenides can react with peroxynitrite and inhibit enzymes from inflammatory pathway which can contribute to their anti-inflammatory properties. Organoselenium compounds can protect brain from glutamate agonists toxicity either by modulating NMDA receptor or by blocking post-receptor activation pro-oxidative events. Ebselen and $(PhSe)_2$ reduce the neurotoxicity of methylmercury related to glutamatergic neurotransmission. Thus the neuroprotective effects of organochalcogenides are mediated by a variety of molecular mechanisms and targets. Of particular importance, since ebselen has not yet entered in clinical use (which can be due to its relative complex and expensive synthesis), the development and the study of the pharmacology and toxicology of simple chalcogenides should be considered an important task for the next years. Particularly, if one considers the low toxicity and the efficacy of diphenyl diselenide in a variety of in vitro and in vivo models of neurotoxicity in rodents.

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