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CHEMOPROTECTIVE ROLE OF DIPHENYL DISELENIDE AND QUERCETIN IN DROSOPHILA MELANOGASTER AND RAT MODELS OF MANGANESE-INDUCED NEUROTOXICITY

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Abstract: There is a growing body of evidence indicating that environmental exposure to metals has severe implication in cognitive function, brain impairment and developmental neurotoxicity in children and adults. For instance excessive exposure to manganese is associated with severe central nervous system dysfunctions otherwise referred to as "manganism." The underlying mechanisms involve the release of reactive oxygen species following metabolism in the cell, mitochondrial dysfunction and altered acetylcholinesterase activity leading to dopaminergic dysregulation of neuronal activity. Neuroprotection afforded by agents with potent antioxidant and anti-inflammatory properties offers a rational and pragmatic approach to neurodegenerative disorders. Diphenyl diselenide and Quercetin owing to their intrinsic antioxidant and anti-inflammatory properties have been reported to play key roles in neuroprotection. In *Drosophila melanogaster* model, exposure of the flies to manganese significantly increased flies mortality, whereas the survivors exhibited significant locomotor deficits with increased acetylcholinesterase (AChE) activity and decreases in antioxidant enzyme activities accompanied with significant increases in the generation of reactive oxygen and nitrogen species. However, dietary supplementation with Diphenyl diselenide (DPDS) caused a significant decrease in mortality, improvement in locomotor activity and restoration of AChE activity in manganese-exposed flies and augmentation in antioxidant status in manganese treated flies. Quercetin improved the neurobehavioral performance of manganese-treated rats confirmed by track and occupancy plot analyses. Specifically, Quercetin prevented manganese-induced locomotor and motor deficits- decrease in total distance travelled, total body rotation, maximum speed, absolute turn angle as well as the increase in time of immobility and grooming. Moreover, quercetin assuaged manganese-induced oxidative damage and perturbation of antioxidant enzymes system and the increase in acetylcholinesterase activity, in the hypothalamus, cerebrum and cerebellum of the rats. Furthermore, quercetin mediated suppression of inflammatory indices and apoptosis which was accompanied by preservation of histo-architectures of the brain, testes and epididymis in manganese treated rats. Taken together, our data demonstrate that DPDS and Quercetin by antioxidant, anti-inflammatory and anti-apoptotic mechanisms may be promising chemopreventive signatures against neurotoxicity resulting from acute manganese exposure.