

Phytochemical Intervention if ROS associated Parkinsons Pathogenesis

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A particular breed of reactive oxygen species have been implicated in the some of the aging-associated havoc caused within the seat of our thinking; the brain. Free radical damage to key housekeeping machinery within dopaminergic neurons is linked to the progress of Parkinson's disease; and within cholinergic neurons, Alzheimer's.

Our overall goals are to understand the role played by intracellular housekeeping machinery in seeding select neurodegenerative disorders. Protein Disulfide Isomerase (PDI) is a housekeeping chaperone involved in intracellular cargo sorting and processing. Recent reports implicate nitrosative stress-induced S-nitrosylation of PDI's catalytic cysteines in promoting the pathogenesis of sporadic Parkinson's and Alzheimer's diseases. In cell line studies, PDI S-nitrosylation was linked to the accumulation of the major and signature Parkinsonian biomarker, alpha-synuclein and to the formation of Lewy neurites. Of therapeutic, albeit limited practical significance, other studies have demonstrated that overexpression of PDI was able to attenuate synphilin-1 accumulation and was found to be neuroprotective, establishing the housekeeping chaperone as an endogenous neuroprotectant. Our laboratory has employed diet-derived polyphenolic architectures to mitigate the incidence of nitrosative-stress-induced Parkinsonian biomarker accumulation. In related studies, we continue to explore practical and theoretical mechanisms toward improving the prophylactic potential of these kitchen therapeutics. Results from these studies will be discussed.