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HARMFUL POTENTIAL OF PREVENTIVE QUERCETIN CONSUMPTION: EFFECTS ON P19 NEURONS

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Oxidative stress, condition induced by accumulation of reactive oxygen species (ROS), has been implicated in brain dysfunction during physiological aging and in various neurodegenerative diseases. A great interest has been directed to natural antioxidants and their potential to regain redox homeostasis and prevent or delay cognitive and motor impairments in humans. Numerous reports of beneficial effects of natural compounds resulted in many commercially available nutraceutical supplements and purified herbal extracts with doses and bioavailability of powerful antioxidants highly beyond levels associated with a typical diet. A growing number of evidence suggests that effects of antioxidants are not exclusively beneficial, particularly at higher doses, thereby questioning safety of prolonged antioxidant consumption.

We studied effects of high doses of quercetin (up to 150 μM), the ubiquitous natural antioxidant and one of the most potent scavengers of ROS from the flavonoid family, on P19 neurons obtained by the differentiation procedure from the P19 mouse embryonal carcinoma cells in the presence of retinoic acid.

Exposure to quercetin for 24 h did not compromise neuronal survival, but morphological examination revealed that network of thick bundles, as well as the number of fine, thin dendritic processes between neurons were reduced. As expected, high doses of quercetin decreased basal levels of ROS and 4-hydroxy-2-nonenal, a product of lipid peroxidation. Quercetin also depleted intracellular glutathione content suggesting that in physiological conditions it could interfere with redox signaling and adaptation to oxidative stress. Additionally, quercetin disturbed transcriptional expression of some key cell-survival regulating genes (Bcl-2, p53 and c-fos), but did not affect nuclear condensation and caspase-3/7 activation, characteristic phenomena related to programmed-cell death cascade.

The obtained results indicate that quercetin-enriched supplements intended for usage in neurodegenerative prevention should be taken with caution. The diversity of quercetin effects and complexity of potential intracellular interactions between affected genes pointed out the necessity for detailed toxicological and pharmacological studies for all quercetin-containing supplements in order to optimize quercetin concentration and time window of administration that will be efficient in neuroprotection, but without side effects.