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BENEFICIAL EFFECT OF POLYPHENOL QUERCETIN AGAINST OXIDATIVE INJURY IN THE CULTURE OF P19 NEURONS IS MEDIATED BY THE PREVENTION OF CASPASE-INDEPENDENT APOPTOSIS

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Introduction: Neuronal loss is a key observation of neurodegeneration implicated in the dysfunctions of the mammalian brain in physiological aging and numerous diseases and injuries. It is hypothesized that a dietary polyphenol supplementation could be an effective therapeutic strategy in minimizing the undesirable neuronal death.

Materials and methods: Effects of ubiquitous flavonoid quercetin on neuronal death induced by exposure to 150 μM hydrogen peroxide (H_2O_2) for 24 hours were studied in the culture of P19 neurons. Reverse transcriptase PCR and western blot analysis were used to monitor changes in Bcl-2, Bax and PARP expression following H_2O_2 treatment. Changes in nuclear condensation were observed by Hoechst staining, while activities of key apoptotic markers caspase-3 and -7, and lactate dehydrogenase (LDH) activity were performed using commercially available assays (Promega).

Results: Exposure to H_2O_2 decreased neuronal viability without changes in plasma membrane integrity, induced changes in chromatin condensation, slightly decreased Bcl-2 expression and moderately increased caspase-3/7 activity. Moreover, H_2O_2 induced strong PARP overexpression without PARP cleavage, altogether indicating a programmed type of cell death distinct from classical apoptosis. Presence of quercetin attenuated the toxic effects of H_2O_2 by preventing chromatin condensation and H_2O_2-induced changes in caspase activity, as well as changes in Bcl-2 and PARP expression.

Conclusion: The obtained results suggest that the neuroprotective effect of polyphenol quercetin is related to its ability to prevent caspase-independent, PARP-dependent programmed cell death cascade. Hence, beneficial effects of quercetin might be assumed for the prevention of oxidative-stress driven neuronal loss in human aging and neurodegenerative diseases.