

A search for protective effects of aqueous extracts of *Pistacia vera* and *Juglans regia* against diabetes induced oxidative and carbonyl stresses in rat hepatocytes

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Background and Aims: Carbonyl and oxidative stress play important roles in the development of diabetic complications and have been shown to be augmented by various natural compounds and pharmacological agents. Nuts are rich sources of bioactive compounds and antioxidants and various beneficial health effects of nuts have been reported. This study was conducted to evaluate the cytoprotective effects of various extracts and bioactive compounds found in nuts for decreasing cytotoxicity, ROS formation, protein carbonylation, mitochondrial and lysosomal membrane damages in cell toxicity models of diabetes related carbonyl and oxidative stress.

Methods: Methanol, ethanol or chloroform were used to prepare crude Pistachio and Walnut extracts, which were then used to screen for in vitro cytoprotection of freshly isolated rat hepatocytes against oxidative stress (hydroperoxide). Also methanolic extract of 50, 100, 150 μ M Pistachio and Walnut were investigated for possible protective effects against carbonyl stress cell death and protein carbonylation in hepatocytes.

Results: The order of protection by nut extracts against hydroperoxide induced oxidative stress was: methanolic extract > Pistachio methanolic extract > Pistachio ethanolic extract > Walnut ethanolic extract > Walnut chloroform extract > Pistachio chloroform extract. Pistachio also protected against glyoxal induced cell death and protein carbonylation, and even elicited protection when added to hepatocytes 30min after the addition of glyoxal. When Pistachio and Walnut were compared for protectiveness against glyoxal induced carbonyl stress in hepatocytes, walnut protected more effectively at 120min. Both compounds also elicited better protection when premixed with glyoxal before addition to hepatocytes, compared to not premixing with glyoxal.

Conclusions: Our results suggest that bioactive nut constituents in the non-lipophilic extracts were more effective than lipophilic extracts for cytoprotection against hydroperoxide induced oxidative stress. Finally Pistachio and Walnut compounds under physiological conditions were likely effective at preventing glyoxal cytotoxicity by trapping glyoxal or reversing early stage carbonylation.

Keywords: Walnut; Pistachio; Oxidative stress; Protein carbonyl; Hydroperoxide; Glyoxal