Pro-oxidant Effect of Flavonoids on the Activity of Paraoxonase 1

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The inverse relationship between dietary flavonoids consumption and cardiovascular diseases may be associated with the ability of flavonoids to attenuate LDL oxidation. Although flavonoids have been employed to prevent against LDL oxidation, their pro-oxidant effect also deserves an attention in respect to untoward property. Here, the possible inactivation of PON1 during the exposure (30 min, 38 ℃) to various flavonoid compounds was examined, and their pro-oxidant effect was compared to their protective action against Cu^{2+}(10 μM)-catalyzed LDL oxidation. The order of pro-oxidant activity was epicatechin gallate > qucertin > luteolin > kaempferol > catechin > morin > epigenin> naringenin, with IC_{50} value of epicatechin gallate, quercetin, kaempferol, and catechin being 12 μM 38 μM, 87 μM, and 150 μM respectively. The prevention by catalase against quercetin-induced inactivation of PON1 suggests that the inactivating action of quercetin may be mediated through the formation of hydrogen peroxide. Generally, there was a good correlationship between inactivating action and antioxidant activity of flavonoids, supporting the notion that the pro-oxidant action of flavonoids may implicate O-dihydroxy moiety. Noteworthy, rutin, a glycosidic derivative of quercetin, failed to inactivate PON1, alluding that the direct interaction between flavonoids and PON1 may be required. Further studies remain to be performed in order to assess the pro-oxidant effect of flavonoids on PON1 in vivo system.

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Neuroprotective effects of gossypin on beta-amyloid- and oxidative stress-induced toxicity in primary cultured rat cortical cells

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Excessive accumulation of beta-amyloid (Aβ) peptides is one of the leading hypotheses to explain neurodegenerative processes in Alzheimer's disease (AD). It has been suggested that Aβ toxicity is associated with increases in reactive oxygen species, whose overproduction may in turn initiate neurotoxic events. The present study evaluated effects of gossypin, 3, 3', 4', 5, 7, 8-hexahydroxyflavone 8-O-beta-D-glucopyranoside, on the toxicity induced by Aβ(25-35)- or oxidative stress in primary cultured rat cortical cells. Its antioxidative action was also examined by cell-free bioassays. The neurotoxicity induced by Aβ(25-35) in cultured cortical cells was significantly inhibited by gossypin. In addition, gossypin was found to concentration-dependently inhibit the oxidative damage induced by xanthine/xanthine oxidase, arachidonic acid, or buthionine (S, R)-sulfoximine, a GSH depleting agent. Furthermore, gossypin strongly inhibited lipid peroxidation in brain homogenates, with the IC50 of 7.3 μg/ml. It also exhibited potent DPPH radical scavenging activity (IC50 = 6.2 μg/ml). These results demonstrate that gossypin exerts protective action against Aβ-induced neuronal damage primarily through its antioxidative action. Based on these results, gossypin may be beneficial in the prevention or treatment of AD.

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