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.

[PA1-36] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

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.

[PA1-37] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Regulatory Effect of Atopic Allergic Reaction by *Carpopeltis affinis*

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We studied the effect of methanol extract of *Carpopeltis affinis* (CA) on atopic allergic reaction. CA dose-dependently inhibited interleukin (IL)-8 and tumor necrosis factor (TNF)-α secretion from the PMA- plus A23187- stimulated HMC-1. CA also dose-dependently inhibited the histamine and β-hexosaminidase release from mast cells. CA had no cytotoxic effect. These results suggest that CA has the inhibitory effect of atopic allergic reaction and this might be useful for clinical application to treat several allergic diseases such as atopic dermatitis.

[PA1-38] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Quercetin 3-O-α-arabinofuranoside protects heart-derived H9c2 cells against oxidative injury through maintaining MMP

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In this study, we investigated whether the cardioprotective effect shown by quercetin 3-O-α-arabinofuranoside extracted from Lindera erythrocarpa against ROS-induced cell death in H9c2 cardiac myocytes. Cell death was induced by BSO, buthionine sulfoximine, which inhibits GSH level and subsequntly increase ROS level. Cell death was quntitatively determined by measuring lactate dehydrogenase (LDH) activity. BSO-induced ROS level and mitochondrial membrnade potentoal (MMP) were measured using 2,7-dichlorofluorescein diacetate oxidation and rhodamine 123.
In H9c2 cells exposed to BSO 10 mM for 24h, LDH release was remarkably increased by 73% compared to that in control (18.7%). From 1 μM to 10 μM of quercetin 3-O-α-arabinofuranoside reduced LDH release and ROS level induced by BSO, in a dose-dependent manner. Cells exposed to BSO showed an early loss of MMP. This decrease in MMP was significantly reversed by treatment with 10 μM quercetin 3-O-α-arabinofuranoside. In conclusion, our results suggest that quercetin 3-O-α-arabinofuranosied can produce cardioprotective effect against ROS-induced cell death through antioxidant effect. This study was supported by a grant of Ministry of Health & Welfare, Republic of Korea. (00-PJ2-PG1-CD02-0018)

[PA1-39] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

The Joins (SKI 306X) study : Effects on Arachidonic acid metabolism pathway and other inflammatory mediators

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Joins (SKI 306X) is now clinically used for the treatment of osteoarthritis (OA). In previous