[PA1-33] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

13(E)-Labd-13-ene-8α,15-diol isolated from Brachyglottis monroi Induces Apoptosis on Human Breast Cancer MDA-MB231 cell line

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The inhibitory effect of 13(E)-Labd-13-ene-8α·15-diol(1), isolated from the ethanol extract of Brachyglottis monroi, on the proliferation of human breast cancer MDA-MB231 cells was examined. Compound (1) at concentration as high as 16㎍/㎖ has inhibited the proliferation of MDA-MB231 and this cytotoxic effect was increased in a time and dose-dependent manners. The mode of cell death induced by (1) was found to be apoptosis, which was judged by the morphological alteration of the cells using DAPI staining and by the detection of DNA fragmentation using agarose gel electrophoresis. As cell death induced by (1) in MDA-MB231 cells show classic apoptosis feature, these results suggest that (1) induces apoptosis on MDA-MB231.

[PA1-34] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Antioxidant Effects of Hirsutanone Derivatives from Alnus Japonica on Copper Mediated human LDL Oxidation

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Subendothelial accumulation of foam cells plays a key role in the initiation of atherosclerosis. These foam cells accumulate in fatty streaks that evolve to more complex fibrofatty or atheromatous plaques. Oxidized LDL may also be involved in atherogenesis by inducing smooth muscle cell proliferation and smooth muscle foam cell generation.
In this study, two kinds of hirsutanone derivatives 1 and 2 were isolated from the methanolic extract of the leaves of Alnus japonica and characterized by their spectroscopic data. We explored the effect of compounds 1 and 2 on Cu^{2+}-mediated human LDL oxidation. Compounds 1 and 2 exhibited significant LDL-antioxidant activity in the thiobarbituric acid-reactive substance (TBARS) assay with IC_{50} values of 1.5 μM and 3.3 μM, respectively. More specifically, LDL incubated with Cu^{2+} had a lag-phase time (the elapsed time before the onset of rapid formation of conjugated lipid hydroperoxides) of 85 min. However, when 2 μM of compounds 1 and 2 were present during incubation, the lag phase time was extended to 151 min and 110 min, respectively.
In conclusion, these compounds from the Alnus japonica have proven to be an antioxidant against lipid peroxidation of LDL. As LDL oxidation is a key event in the formation of early atherosclerotic lesion, the use of these natural antioxidant may be proven beneficial to attenuate atherosclerosis.

[PA1-35] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

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]