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Nitric oxide (NO) has been reported to play an important role as an effector molecule in cytokine signal transduction in cardiomyocytes. The treatment of IL-1b/ TNF-a (2 ng/ml)/ IFN-g (50 U/ml) induced apoptosis in neonatal rat ventricular cardiomyocytes via NO-dependent pathway. When cardiomyocytes were treated with IL-1b (20 ng/ml)/TNF-a (2 ng/ml)/ IFN-g(50 U/ml) in the presence of catalase, the cells were much more resistant to the cell death as well as NO synthesis. However, catalase significantly enhanced the expression of iNOS protein in cardiomyocytes. This study also showed that catalase rather stimulates the NF-kB binding affinity. However, NO synthase activity is abolished by exogenous catalase, suggesting that H_2O_2 be involved in NO synthesis in a post-translation state. Catalase-induced inhibition of NO was partially but significantly reversed by H_4B, an important cofactor of NO synthesis. In addition, catalase activity was significantly down-regulated by H_4B in a dose-dependent manner. These results suggest that catalase may interfere with the production of NO and with the related apoptosis of cardiomyocytes. This study also shows that catalase-induced inhibition on NO release may be reversed by H_4B by direct interaction between catalase and H_4B.

[PA1-18] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Antihypertensives affects on the drug metabolism of buprenorphine

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Buprenorphine(BPN) is used to treat withdrawal syndromes in narcotic addictions. When narcotics are stopped, withdrawal syndromes such as pupil dilation and blood pressure increment are appeared. And BPN is often prescribed concomitantly with antihypertensives. We researched whether combined medicines of BPN and antihypertensives affected on the metabolism of BPN. After BPN was incubated with antihypertensives such as nifedipine, verapamil, captopril and propranolol in rat or human microsomes, amounts of BPN and its metabolite, norbuprenorphine (NBPN), were measured. NBPN was decreased dose-dependently to 60.5, 51.9, 40.3, 21.6, 12.9% in humans and to 39.5, 28.6, 23.5, 13.1, 6.2% in rats, when the nifedipine was treated with concentrations of 0, 40, 80, 160, 320M. It was also decreased dose-dependently to 72.8, 39.3, 33.9, 30.7, 26.8, 19.3% in humans and to 44, 26.7, 21.5, 18.9, 13, 6.2% in rats, when the verapamil was treated with concentrations of 0, 0.16, 0.32, 0.64, 1.28, 2.56mM. However the captopril and the propranolol had no effects. It showed that calcium channel antagonists such as nifedipine and verapamil suppressed the metabolism of BPN

[PA1-19] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Anti-stress effect of Choa pyroligneous liquid in SD rats.

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Pyroligneous liquid is produced by process carbonizing Oak in 350~400℃. There are 200 kinds of constituents including minerals, vitamin B-complex and organic acids in it. The organic acids of them were presumed as active materials. It is traditionally used for treatment of stress related disorder, hepatic disease, immune disorder, G-I disorder and inflammatory disease. The aim of this study was to investigate anti-stress effects of Pyroligneous liquid(Pyroligneous liquid produced from Choa company). The experiments were performed with the use of young(8 weeks of age) male rats of SD strain weighing between 180 and 220 g at the time of first treatment with Pyroligneous liquid. They were grouped normal, control, Ginseng, diazepam and Pyroligneous liquid group. The normal ones were provide normal water and not exposed to stress. The control ones were provide normal water and exposed to stress. Ginseng, diazepam and Pyroligneous liquid were orally administered Ginseng extract 50㎎/㎏, diazepam 0.5 ㎎/㎏ and Pyroligneous liquid 2㎖/㎏ once a day for 12

days and exposed to stress for 5 days. They were stressed by immobilization for 30 minutes and electro-shock(5㎃/20 secs) for 5 minutes. At first, they were pretreated with Ginseng extract, diazepam and Pyroligneous liquid for 7 days, and followed by the treatments in combination with the exposure to stress for 5 days. We recorded stress related behavioral changes of experimental animals induced by over stress using Etho-vision system. Total activity, rearing, smelling activity, plus maze moved distance, and plus maze-open area duration decreased by stress were increased by treatment of Pyroligneous liquid. Freezing and burrowing activity, and plus maze-staying time in closed area increased by stress were decreased by treatment of Pyroligneous liquid. These results suggest that Pyroligneous liquid protect partially the living organism from stress attack in some case.

[PA1-20] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

C/EBPβ and Nrf2-Mediated GSTA2 Induction by α-Lipoic acid, an Insulin-Sensitizing Agent that has Antioxidant and Prooxidant Activities

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The protective adaptive response to electrophiles and reactive oxygen species is mediated by enhanced expression of phase II detoxifying genes including glutathione S-transferases. α-Lipoic acid, which exerts prooxidant or antioxidant activities, has been shown to activate the insulin signaling pathway and thus to induce insulin-like actions via PI3-kinase and Akt. Our previous studies have shown that PI3-kinase plays an essential role in Nrf2- or C/EBPβ-mediated glutathione S-transferase A2 (GSTA2) induction. This study investigated whether α-lipoic acid induces GSTA2 and, if so, what the role of C/EBPβ and Nrf2 in GSTA2 induction by α-lipoic acid. Western blot analyses showed that α-lipoic acid at the concentrations of 100 μM or above increased the GSTA2 protein levels in H4IIE cells at 12 h or later times. In α-lipoic acid (100 μM)-treated cells, the intensity of nuclear protein(s) binding to the consensus sequence of C/EBP (TTGCGCAA) increased and C/EBPβ translocated to the nucleus. Nuclear Nrf2-ARE complex was activated 30 min-1 h after treatment of cells with α-lipoic acid. α-Lipoic acid treatment increased luciferase reporter-gene activity in H4IIE cells transfected with the plasmid containing −1.65 kb flanking region of the GSTA2 gene. Deletion of either the C/EBP binding site or the ARE substantially abolished the reporter gene activity, indicating that activation of C/EBPβ and Nrf2 both contributed to GSTA2 induction by α-lipoic acid. Insulin enhanced the induction of GSTA2 by α-lipoic acid, which was accompanied by the increase in C/EBPβ binding to its DNA binding site. By contrast, the induction of GSTA2 by α-lipoic acid was attentuated by concomitant treatment of cells with N-acetylcysteine an antioxidant. These results demonstrated that α-lipoic acid induces GSTA2 via activation of both C/EBPβ and Nrf2 and that C/EBPβ and Nrf2 activation by α-lipoic acid may have resulted from the insulin signaling pathway and the prooxidant activity.

[PA1-21] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Inhibitiory effect of green tea extract on Aβ-induced PC12 cell death

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Beta-amyloid peptide (Aβ) is considered to be responsible for the pathogenesis of the Alzheimer's disease. Several lines of evidence support that Aβ-amyloid-induced cytotoxicity is mediated through the generation of reactive oxygen species (ROS). Agents that are able to scavenge excess ROS may be useful as protecting or reducing agents for development or progress of AD. Green tea extract has been known to have antioxidant property. Our previous studies also demonstrate that green tea extract protected ischemia/reperfusion-induced brain injury by reduction of cell death through scavenging of oxidative damages of macromolecules. In this study, we have investigated the effects of green tea extract on Aβ-induced oxidative cell death in cultured cortical neurons and rat pheochromocytoma (PC12) cells. Cerebral cortical neurons and PC12 cells treated with Aβ (10,