induced aging. Moreover, inflammation and cirrhosis in liver tissue of CS treated group were significantly decreased.
These results suggest that CS might be a useful candidate for antioxidative reagent.

[PA4-13] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Preventive Effect of Saponins from Puerariae Radix and Panax Ginseng on the Hepatotoxicity

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Puerariae Radix and Panax Ginseng are used in traditional oriental medicine for various medicinal purposes. Preventive effects of saponins obtained from Puerariae Radix and Panax Ginseng on the hepatotoxicity in CCl4-treated rats were studied.
The antioxidative effects of Panax ginseng saponin(PGS) and puerariae radix saponin(PRS) were investigated at the levels of liver tissue total homogenates, mitochondrial and microsomal fractions of SD-rats intoxicated with carbon tetrachloride(CCl4).
Lipidperoxides of each fraction in ANO group were highly increased compared to NO group. Extracts of Panax Ginseng and Puerariae Radix treated group markedly inhibited lipidperoxidation by 47 % ~ 75 %.
And as the result of the measurement of SOD (superoxide dismutase), catalase, total glutathione (GSH +GSSG) and glutathione peroxidase (GPx) activities in the liver tissue total homogenates, mitochondrial and microsomal fractions were highly decreased in ANO group compared to NO group.
But they were increased significantly in the PGS, PRS groups compared to ANO group.
Especially, catalase, total glutathion and GPx activities in microsomal fractions of ANO group were highly showed.
And also, SOD activity in mitochondrial fraction of ANO group actively decreased compared to in microsomal fraction and liver tissue total homogenetes of ANO group.
In view of this study PGS, PRS were effective on the detoxication of liver injury.

[PA4-14] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Anti-tumor Agent, Paclitaxel, Induces *de novo* Synthesis of Ceramide, Which May Lead to Apoptosis in Human Breast Cancer MCF-7 Cells

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The anti-neoplastic agent paclitaxel (Taxol), a microtubule stabilizing agent, is known to arrest cells at the G2/M of the cell cycle and apoptosis. Although much is known about cytotoxic mechanisms, the effect of paclitaxel cannot be solely explained by microtubular interation. Several reports recently demonstrated that ceramide, a second messenger in apoptotic signaling, plays a key role in the nature of cellular response to anti-cancer therapies, participating in reactions to both chemotheraphy and radiation. This study was undertaken to determine whether ceramide production is involved in paclitaxel-induced apoptosis in human breast cancer cells. Exposure of cells to paclitaxel resulted in the enhanced production of ceramide, which is reduced by two inhibitors of sphingolipid biosynthesis, fumonisin B1, a ceramide synthase inhibitor, and L-cycloserine, a serine palmitoyltransferase inhibitor. An inhibitor of glucosylceramide synthesis, 1-phenyl-2-dacanoylamino-3-morpholino-1-propanol, induced ceramide production. Importantly, L-cycloserine significantly attenuated paclitaxel-induced cell death in MCF-7 cells. These results suggest that paclitaxel-induced apoptosis is, in part, attributable to ceramide and

sphingoid bases. Clinical use of paclitaxel may maximize its cytotoxic potential through its ceramide-producing activity.

[PA4-15] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Ceramide Is Linked to Glutamate-induced Cell Death in Cultured Cortical Neurons

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Glutamate is known to play a pivotal role in the pathogenesis of epileptic seizure, brain injury associated with stroke and trauma as well as in neurodegenerative disease such as Alzheimer's disease, Huntington's chorea and Parkinson's disease. While excessive activation of glutamate receptor is responsible for neuronal injury, glutamate has, recently, been known to induce apoptosis in cultured rat neocortical neurons. Thus far, overstimulation of glutamate receptors has been known to induce intracellular calcium overload, which activates a cascade of cytotoxic biochemical events leading to necrotic neuronal death. However, the mechanism by which glutamate induce such neuronal apoptosis has not been fully understood. Here we for the first time report that ceramide was increased by treatment of glutamate to the primary cortical neurons with a concomitant decrease in sphingomyelin and may be responsible for the neuronal apoptosis. The cortical neurons contain a neutral form of N-SMase as a major SMase activity, whose activity was rapidly and stably enhanced by glutamate. Furthermore, MK801, an antagonist of glutamate receptor, significantly blocked these biochemical and cellular events. Our data suggest that glutamate-induced neuronal apoptosis could be provoked by ceramide produced through activation of a neutral form of N-SMase.

[PA4-16] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Phosphatidylcholine-specific Phospholipase C-mediated Activation of Acidic Form of Sphingomyelinase May Lead to Methylmercury-induced Cell Death

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Methylmercury (CH_3HgCl) is the most important form of mercury in terms of toxicity and health because of its high level of bioconcentration through aquatic food chains. Although this compound has been known to affect various organs including brain and kidney, the mechanism remains poorly understood. In this work, the biochemical events associated with cell death induced by CH_3HgCl have been analyzed in Madin Darby Cannine Kidney (MDCK) cells. Results indicate that CH_3HgCl-induced cell death is attributable to an early ceramide generation caused by the activation of an acidic spingomyelinase (A-SMase). Moreover CH_3HgCl treatment rapidly induces diacylglycerol (DAG) generation through activation of phosphatidylcholine-specific phospholipase C (PC-PLC), an event which preceeds and is required for A-SMase activation. Moreover A-SMase activity, but not neutral form of SMase, was stably enhanced by exposing MDCK cells to CH_3HgCl. Indeed, PC-PLC inhibition by D609 totally prevented CH_3HgCl-induced A-SMase activity, ceramide generation and consequent cell death. These observations indicate that CH_3HgCl induces MDCK cell death through the sequential activation of PC-PLC and A-SMase, and early ceramide generation.

[PA4-17] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]