whether ceramide formation plays a role in hypoxia-induced apoptosis. Ceramide level was measured in SH-SY5Y human neuroblastoma cells by metabolic labeling with [^{3}H]palmitic acid or [^{3}H]serine. Hypoxia resulted in the increase in ceramide production with subsequent evidence of apoptosis in SH-SY5Y cells. Both fumonisin B1 (FB1), a ceramide synthase inhibitor, and L-cycloserine, a serine palmitoyltransferase inhibitor, blocked hypoxia-induced ceramide generation while sphingomyelin levels remained unchanged. L-cycloserine, but not FB1, reduced hypoxia-induced apoptosis. This may be due to a known cytotoxic sphingolipid, sphinganine accumulated by cotreatment of hypoxia and FB1. Hypoxia-induced cell death and ceramide production were significantly potentiated by NOE (N-oleoylethanolamine), an inhibitor of ceramidase, and PDMP (DL-thero-1-phenyl-2-decanoylamino-3-morpholino-1-propanol), an inhibitor of glucosylceramide synthase (GCS). PARP cleavage and caspase 3 activation were accelerated and potentiated by treatment of PDMP but not NOE. This indicated that GCS is more important in hypoxia-induced apoptosis than ceramidase. Hypoxia-induced neuronal cell death was potently inhibited by an inhibitor of caspase, z-VAD-fmk (z-VAD-fluoromethylketone). Our results suggest that hypoxia-induced neuronal cell death may be caused by increase in the *de novo* synthesis of ceramide pathway and the subsequent activation of caspase.

Poster Presentations - Field B1. Physiology

No submitted abstract in the field B1 (Physiology)

Poster Presentations - Field B2. Pathology

[PB2-1] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Anti-proliferative Effects of Godulbaegi Extracts on Human Cancer Cells

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We investigated the anti-proliferative effects of godulbaegi (*Ixeris sonchifolia* H.) root extracts, luteolin (3', 4', 5, 7-Q-glucoside and 3', 4', 5, 7-tetrahydoxyflavone) and apigenin (3', 4', 5, 7-O-gluconic acid) on SK-MEL-2 human melamine cancer cells and HepG2 liver cell line. In MTT assay 3', 4', 5, 7-tetrahydoxyflavone showed the most efficient anti-proliferative effects. According to PI staining and DNA fragmentation assay, we postulated that this effects may be a result from cell cycle arrest, then we examined the changes of protein expression related cell cycle arrest and apoptosis. Western blotting data represented that the expression of p53, cyclin A and cyclin B1 were decreased against the increase of quantity of 3', 4', 5, 7-tetrahydoxyflavone in HepG2 cell line. However, luteolin induced apoptosis in SK-MEL-2 cells. Now we are performing more experiments to clear the potentiality of it's cell cycle arrest and/or apoptosis inducing effects on human cancer cells.

[PB2-2] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Inhibitory Action of Phenylpropanoids on Phospholipase A2 Activity in RAW 246.7 Cells

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Phenylpropanoids which are widely distributed in vegetable kingdom, have anti-inflammatory activity on carrageenan-induced rat paw edema. Their mechanisms are not clear. In this study, to find out their mechanism, effect of phenylpropanoids on phospholipase A2 (PLA2) activity were examed in the silica-induced [3H]arachidonic acid release in RAW 246.7 cells. Silica stimulated PLA2 activity in a dose dependent manner. Phenylpropanoids have dose-dependently decreased the [3H]arachidonic acid release in RAW 246.7 cells. Silica-induced PLA2 activity was significantly inhibited by sinapinic acid and quinic acid at a concentration of more than 10 μM, but was not affected by other phenylpropanoids, such as cinnamic acid, p-coumaric acid, caffeic acid, ferulic acid and chlorogenic acid at 100 μM. It shows that quinic acid has the most activity. Quinic acid and sinapinic acid at a concentration of 10 μM decrease significantly the [3H]arachidonic acid release in RAW 246.7 cells. These results indicated that the more has hydroxy group of benzene ring, the more has potent inhibitory activity of phospholipase A2 activity.

[PB2-3] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Inhibitory Action of Phenylpropanoids on Silica-induced Reactive Oxygen Species Generation in RAW 246.7 cells

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Silica which is a typical fibrogenic particles in many occupations including coal mining, quarrying and sandblasting induced acute inflammatory response and fibrosis in lung. we reported that structure-activity of phenylpropanoids on anti-inflammatory activity on carrageenan-induced rat paw edema. Their mechanisms are not clear. In this study, to find out their mechanism, effect of phenylpropanoids on reactive oxygen species (ROS) generation were examed in RAW 246.7 cells. Silica stimulated ROS generation in a dose dependent manner. Phenylpropanoids have dose-dependently decreased ROS generation in RAW 246.7 cells. It shows that chlorogenic acid has the most activity. Chlorogenic acid and caffeic acid at a concentration of 1 μM decrease significantly ROS generation, and also ferulic acid and sinapinic acid at a concentration of 10 μM decrease significantly ROS generation in RAW 246.7 cells. These result indicated that cinnamic and p-coumaric acid has not active, but the more has hydroxy group of benzene ring, the more has potent inhibitory activity of ROS generation.

[PB2-4] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Inhibitory Action of Cinnamic Acids Derivatives on Silica-induced Peroxynitrite Generation in RAW 246.7 Cells

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C6-C3 compound, cinnamic acid derivatives are widely distributed in vegetable kingdom. Recently, we reported that structure-activity of cinnamic acid derivatives on anti-asthmatic activity in the increase of specific airway resistance of ovalbumin-sensitized guinea pig and anti-inflammatory activity on carrageenan-induced rat paw edema, respectively. Their mechanisms are not clear. In this study, to find out their mechanism, effect of cinnamic acid derivatives on peroxynitrite (PON) generation were examined in RAW 246.7 cells. Silica stimulated PON generation in a dose dependent manner. Cinnamic acid derivatives have dose-dependently decreased PON generation in RAW 246.7 cells. It shows that ferulic acid has the most activity. Ferulic acid, caffeic acid and chlorogenic acid at a concentration of 1 μM decrease significantly PON generation, and also quinic acid, coumaric acid and sinapinic acid at a concentration of 10 μM decrease significantly PON generation in RAW 246.7 cells. These result indicated