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Aconiti Tuber is the root of *Aconitum* sp(Ranunclaceae) which has been considered as one of the most important herbal medicine having diuretic and analgesic effect. But it has been well known that A. Tuber contained toxic compounds, aconitine alkaloids so that only processed A. tubers have been used as herbal drug traditionally.
For the investigation of Aconiti Tuber toxicity on Liver, Kidney cell lines, the commercial processed Aconiti Tuber which is called as Yumbuja was more processed into four kinds of processing methods after Chinese Pharmacopoeia and other traditional medicine literatures and these five processed drugs were extracted with hot water.
Processing methods
①. Blanch the commercial processed Aconiti Tuber -Yumbuja- with water, 2-3 times a day until all salt is rinsed out. Boil together with Radix Glycyrrhizae, black beans and water until the centre of the cut surface is devoid of white core and cut slice is numbless to the tongue. remove Radix Glycyrrhizae, black beans, cut the drug into slices, and dry in the sun. (To each 100kg of Ryumbuja add 5kg of Radix Glycyrrhizae and 10kg of black beans)
②. Blanch the commercial processed *Aconiti Tuber* -Yumbuja- with water, 2-3 times a day until all salt is rinsed out. Boil together with water until the centre of the cut surface is devoid of white core and cut slice is numbless to the tongue. cut the drug into slices, dry in the sun.
③. Blanch the commercial processed Aconiti Tuber -Yumbuja- with water, 2-3 times a day until all salt is rinsed out. Treat it on 120℃, for 40 minutes in dry oven, and cut into slices and dry in the sun.
④. Treat the commercial processed Aconiti Tuber -Yumbuja- on 120℃, for 40 minutes in vacuum oven, cut into slices and dry in the sun.
In Vitro test(MTT assay on Vero 76 and NCTC clone 1468)
The toxicities of hot H2O extracts of five processed drugs were evaluated on the two kinds of 2 x 105 cell line(Vero 76: kidney cell, NCTC clone 1469: liver cell) by MTT assay. The vero 76 cells showed no or very weak toxicities of all processed drugs in concentration of 0.18 - 0.5mg/200㎕, but the NCTC clone cell showed IC50 in concentration of 12-20㎍/200㎕. Especially, IC of Yumbuja was the lowest of all (12㎍/200㎕). From this data, it suggested that the prossesed Aconiti Tuber could be decreased toxicity in kidney cell, but these processing methods may not help to decrease of liver toxicity.
In Vivo test(Acute toxicity in mice)
For the investigation of A. tuber toxicity, hot water extracts from five kinds of processed A. Tuber were tested in mice one time oral administration in 5 different dosis(2.0g/㎏, 2.6g/㎏, 3.2g/㎏, 4.0g/㎏, 5.0g/㎏). Their LD50 values were above 4-5g/㎏.

[PA4-12] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Antiaging effect of CS in ovariectomy induced rat liver

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The ovarian hormone deficiency induced ovariectomy rat is widely used as aged model due to its practicality, convenience, and cost effectiveness. The surgically ovariectomized rat induces aging by reactive oxygen species(ROS) generation.
Reduced cartilage Chondroitin Sulfate(CS), a component of articular cartilage proteoglycan, levels may be a risk factor involved in articular cartilage in elderly people.
To investigate the deaging effects of intraperitoneally injected CS on various antioxidative enzyme activity (Malondialdehyde (MDA), Superoxide Dismutase (SOD), Catalase (CAT), reduced-Glutathione (GSH), oxidized-Glutathione (GSSG), Glutathione Peroxidase (GPx)) and histopathology of liver tissue, ovariectomized rats were used.
The antioxidative effects of CS(100㎎/㎏ and 200㎎/㎏ body weight) were investigated by the antioxidative enzyme activities of liver homogenate fractions (liver total homogenate, mitochondrial, and microsomal fractions). In addition, the ovariectomized rat liver was histologically examined.
Intraperitoneally injected CS, dependent on dosage, indicated a protective effect against ovariectomy-

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