[PA4-14] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Colchicine poisoning

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Colchicine is a drug well known for its use in the therapy of acute attacks of gouty arthritis. Two death caused by oral ingestion of colchicine was reported. Two persons were all women. The one was 34 years old woman and with his boyfriend in a inn and the other was a housewife. The first one was a alcoholic but his boyfriend was afflicted with gout. So her boy friend carried over about 60 tablets of colchicine, 4 tablets of naltrexone and 22 tablets of fluoxetine. After her death there were remained colchicine 2 tabs, naltraxone 4 tabs and fluoxetine 22 tabs. We deduced that she ate her boy friend's colchicine about 58tabs with alcoholic drink. But when we met her blood, there was no alcohol but colchicine was detected in her blood. The blood concentration of colchicine was 0.2㎍/㎖. The second woman was not a alcoholic but she drank alcohol with her husband. After that she had a quarrel with her husband. She was placed under medical care for her ingestion of drug before her death. But in her blood there was no alcohol and colchicine. Colchicine in blood was extracted by liquid extraction. we analysed the colchicine with HPLC/PDA.

[PA4-16] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Different mechanisms mediate uptake of lead in a rat glial cell line

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The mechanism by which lead enters glial cells was examined. The uptake of lead reached saturation when assays were performed in buffers at pH 5.5 and 7.4. The Vmax and Km was 2.7 pmoles/mg protein/min and 13.4 M in the buffer at pH 7.4, respectively, whereas the Vmax and Km was 329 fmoles/mg and 8.2 M in the buffer at pH 5.5, respectively. Uptake in a buffer at pH 5.5 but not at pH 7.4 was inhibited by iron. Cells treated with the iron chelator desferoxamine displayed higher levels of the divalent metal transporter mRNA and protein. Cells treated with desferoxamine displayed greater uptake of lead in the buffer at pH 5.5 but in the buffer not at 7.4. The transport of Pb was blocked by the anion transporter inhibitor 4,4-diisothiocyanatodihydrostilbene-2,2-disulfonic acid (DIDS) in the buffer at pH 7.4, which bound to cell surface proteins at concentrations that were similar to those that blocked Pb uptake. DIDS did not inhibit uptake in the buffer at pH 5.5. Greater uptake of Pb was observed in a buffer containing sodium bicarbonate, which was inhibited by DIDS. When the uptake of Fe, Mn, and Zn was examined, only uptake of Zn was inhibited by DIDS. In summary, glial cells display two distinct transport mechanisms for Pb that are distinguishable by their sensitivity to inhibitors and activators at pH 5.5 and pH 7.4 in glial cells.

[PA4-17] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

New HDAC inhibitor, IN2001 induces apoptosis/cell cycle arrest in human breast cancer cells

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The acetylation of histone is one of the mechanisms involved in the regulation of gene expression and is tightly controlled by two core enzymes, histone acetyltransferase (HAT) and deacetylase (HDAC). There are several reports that imbalance of HAT and HDAC activity is associated with abnormal behavior of the cells in morphology, cell cycle, differentiation, and carcinogenesis. Recently, an increasing number of structurally diverse HDAC inhibitors have been identified that inhibit proliferation and induce differentiation and/or apoptosis of tumor cells in vivo and in vitro. In this study, we have investigated the effects of novel HDAC inhibitors, IN2001 on ER positive and ER negative human breast cancer cell lines. The growth inhibition, cell cycle arrest and apoptosis of cells by HDAC inhibitors were determined using SRB assay, DNA fragmentation, and flow

cytometry. We found that IN 2001 as well as Trichostatin A inhibited cell growth dose-dependently in both ER positive and ER negative human breast cancer cell lines. The growth inhibition with HDAC inhibitors was associated with profound morphological change. The result of cell cycle analysis after 24 h exposure of IN2001 showed G2-M cell cycle arrest in MCF-7 cell and apoptosis in T47D and MDA-MB-231 cell. In summary, IN2001 has antiproliferative effect on human breast cancer cells regardless of the expression of estrogen receptor. These findings heights the possibility of developing HDAC inhibitors as potential anticancer therapeutic agents for the treatment of breast cancer.

[PA4-18] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Micronucleus test of SS cream and CJ-4001 using Acridine orange staining method

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SS cream and its revised formula, CJ-4001 is topical Chinese herbal drugs for premature ejaculation. To evaluate the genotoxic potentials of these drugs, micronucleus test using Acridine orange (AO) staining method was performed. Acridine orange (AO) staining is adopted in OECD guideline 474 and widely used in micronucleus test. In dose range finding study, no mouse was dead at 2000 mg/kg using single treatment subcutaneously. Therefore, 3 dose levels were chosen at 500, 1000, 2000 mg/kg. ICR male mice were subcutaneously administered with SS cream and CJ-4001 at doses of 500, 1000, 2000 mg/kg. Mytomycin C (MMC, 2 mg/kg) used as positive control was injected intraperitoneally. Bone marrow was collected from femur at 24h following the injection. Samples were stained according to AO staining method and 2,000 polychromatic erythrocytes (PCEs) were observed per mouse. As a result, the frequency of micronucleated polychromatic erythrocyte (MN-PCE) was 1.8±1.3 and 29.0±7.4‰ at vehicle control and MMC-treated group, respectively. MN-PCE frequency in SS cream-treated group was 1.3±0.8, 1.0±0.9, and 1.0±0.9‰ at doses of 500, 1000, 2000 mg/kg, respectively. MN-PCE frequency in CJ-4001-treated group was 0.3±0.6, 0.5±0.5, and 0.3±0.6‰, respectively. In conclusion, SS cream and CJ-4001 were negative at micronucleus test in mice.

[PA4-19] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Fatal cases related to propofol

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Propofol(2,6-diisopropylphenol) is rapid, short-acting intravenous anaesthetic agent. It is used for the induction and maintenance of general anaesthesia or sedation. The recommended doses are 2-2.5mg/kg given as a titration infusion over about 30min to achieve anaesthesia. Recently, we encountered 4 fatalities related to propofol. One death is a suicide by self-administered of propofol and the others are therapeutic misadventures during surgical care. The propofol level in the blood and tissues were determined by gas chromatographic analysis with mass spectral detection. In suicidal case, blood concentration of propofol was 5.1㎍/㎖ and higher than those of accidental case (0.2㎍/㎖, 0.3㎍/㎖, 1.1㎍/㎖). In one fatal case by misadventure, the propofol levels in kidney, brain and adipose tissues were 1.8㎍/㎖, 1.2㎍/㎖ and 4.5㎍/㎖ respectively. Those were higher than blood level (1.1㎍/㎖) because of rapid metabolism and distribution of propofol to the tissues.

[PA4-20] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Rapid Screening Method for the Solid-Phase Extraction and GC/MS analysis of Diazepam.

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