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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Diazepam (DZ) is one of the most frequently prescribed drugs as an antianxiety agent, muscle relaxant, and anticovulsant and sometimes causes intoxication due to accidental overdose, misuse or abuse. Screening or confirmation methods for DZ and NDZ in plasma are very important for clinical and toxicological studies and in forensic cases. GC/MS assay with SPE was developed for the determination of diazepam and its metabolite, nordiazepam in human plasma. Diazepam in plasma was extracted by a rapid and sensitive procedure based on C18 bonded-phase extraction. GC/MS analysis was performed using a Agilent MSD 5973 mass spectrometer and the column was a DB-5MS. The detection limit was 0.5 ng/mL and the assay was sensitive to 1 ng/mL and linear to 3000 ng/mL with correlation coefficients of >0.99 for both DZ and NDZ. The recoveries of DZ and NDZ were >80.0. The within-run CVs and between-run CVs of diazepam and nordiazepam were less than 10%. This sensitive and simple method is useful for plasma samples of forensic toxicological interest and in clinical studies when low concentrations of DZ are to be detected.

[PA4-21] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Identification and semi-quantitation of dextromethorphan and its metabolite in urine using the REMEDi HS system

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To determinate dextromethorphan (DMP) and its active metabolite dextrorphan (DRP) in urine was performed using REMEDi™ (Rapid EMErgency Drug identification) that is a fully automated multicolumn high performance liquid chromatographic (HPLC) system with a scanning ultraviolet detector. The limits of detection for DMP and DRP were 0.10 and 0.15 μg/mL, respectively. The standard curves were linear, with correlation coefficients ($r > 0.975$) in the concentration range of 0.5 ~ 10.0 μg/mL. The accuracy was 66.4 ~ 82.4% and 66.7 ~ 85.6%, and the precision was 1.3 ~ 7.8% (coefficient of variance, CV) and 0.9 ~ 7.8% (CV) for each of the compounds. The DMP and its metabolite DRP in urine samples were rapidly identified and semi-quantitated by REMEDi without any sample pretreatment.

[PA4-22] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Regulation of CYP 1A1 gene expression by retinoic acid receptor, retinoid X receptor and constitutive androstane receptor in rainbow trout hepatoma cells(RTH 149)

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Exposure of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) causes a variety of biological and toxicology effects, most of which are mediated by aryl hydrocarbon receptor (AhR). The ligand-bound AhR as a heterodimer with AhR nuclear translocator (ARNT) binds to its specific DNA recognition site, the dioxin-responsive element (DRE), and it results in increased transcription of CYP1A1 gene. Retinoic acid (RA) regulates the transcription of various genes for several essential functions through binding to two classes of nuclear receptors, the retinoic acid receptor (RAR) and retinoid X receptor (RXR). Constitutive androstane receptor (CAR) also regulates the transcription of gene. In this study, we have examined how RAR, RXR and CAR regulated CYP1A1 in rainbow trout hepatoma cell (RTH 149) using luciferase reporter gene assay system. We did transient transfection with CYP1A1 luciferase reporter gene and treated with TCDD, all-trans RA, 9-cis RA and phenobarbital. Treatment of all-trans RA, 9-cis RA or phenobarbital decreased the TCDD induced transcription of CYP1A1. When we did transient cotransfection with CYP1A1 luciferase reporter gene and RXR, as increase of RXR concentration, the TCDD induced transcription of CYP1A1 was decreased. Transfection with CAR also decreased the TCDD induced transcription of CYP1A1 in RTH 149 cells.

[PA4-23] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]