Sildenafil, an oral therapy for erectile dysfunction is sold by the name of ViagraTM. It has a potential for cardiac risk of sexual activity in patients with preexisting cardiovascular disease. Therefore, sildenafil citrate should not be generally used in men for whom sexual activity is inadvisable because of their underlying cardiovascular status. There was a case of death related with sildenafil. He was dead shortly after sexual intercourse. He was the director of Taekwondo and 61 years old. He was-supposed to have been taken drugs related with hypertension and thrombotic disease because he had some of terazocin and aspirin. he also had 2 tablets of Viagra among 4 tablets packing. It was deduced that he ate 2 tablets of Viagra. Each tablet of Viagra has 100 mg of sildenafil. We analyzed sildenafil with HPLC/PDA detector from post-mortem blood. There wasn't any other drugs in blood except sildenafil but aspirin was also detected in gastric juice. Sildenafil concentration in blood was 0.3㎍/㎖.

[PA3-2] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Report on the Modified Sildenafil

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Sildenafil ((1-[4-ethoxy-3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo-[4,3-d] pyrimidin-5yl) phenylsulphonyl]-4-methylpiperazine) is an oral therapy used for male erectile dysfunction(MED). Despite the efficacy of sildenafil as treatment for MED, there are some notable drawbacks in patients with preexisting cardiovascular disease. Therefore. sildenafil citrate (Viagra^{TM}) is a prescription medication available only from doctors and should be done with caution. As Its effects on MED have been known, many counterfeits which contain sildenafil have been dealed in illegally such as the formulation of tablets, capsules and drinks. We analyzed counterfeit sildenafil with HPLC/PDA. Almost all counterfeits had sildenafil, but some sample such as a capsule, a decoction and liquid raw materials, contained modified sildenafil that had some different retention time in HPLC. This substance showed a molecular ion peak at 14 mass unit higher than that of sildenafil in LC/MS-analysis. Through NMR, we confirmed the detail structure as methylated sildenafil analogue on piperazine ring. We don't know whether this substance has sildenafil-like effects on MED, so its activity assay must be done.

[PA3-3] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

A Novel Antithrombotic Agent, NQ304 Inhibits the Proliferation of Vascular Smooth Muscle Cells

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Several 1,4-naphthoquinone derivatives have been reported to possess many pharmacological effects such as anti-viral, anti-fungal, anti-cancer and anti-platelet activities. However, little has been known about functional role in vascular smooth muscle cells (VSMCs). Among the synthetic 1,4-naphthoquinone derivatives, we found that 2-chloro-3-(4-hexylphenyl)-amino-1,4-naphthoquinone (NQ304) is a potent growth inhibitor on VSMCs. In this study, a possible anti-proliferative mechanism of NQ304 on rat aortic VSMCs was investigated. NQ304 (1-10 μM) significantly inhibited 5% fetal bovine serum (FBS)-induced proliferation of rat aortic VSMCs evaluated by direct counting of cell number and [^{3}H]-thymidine incorporation assay. There was no evidence of cellular toxicity or apoptosis of NQ304 (10 μM) as determined by trypan blue exclusion assay, flow cytometric analysis and DNA fragmentation assay. The intracellular signaling effect of NQ304 on the FBS-induced activation of extracellular signal-regulated kinase 1/2 (ERK 1/2) and Akt cascade by western blot and electrophoretic mobility shift assay (EMSA) in cultured VSMCs were also examined. Pre-treatment of VSMCs with NQ304 resulted in a significant inhibition of the FBS-induced phosphorylation of ERK1/2 and Akt kinase. These results indicate that NQ304 may inhibits vascular smooth muscle cell proliferation through blocking of ERK 1/2 and Akt cascade.

[PA3-4] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]