arsenic affects vasomotor tone in blood vessels, we investigated the effect of arsenic on agonist-induced vasorelaxation using the isolated rat aortic rings in in vitro organ bath system. Treatment with arsenite inhibited acetylcholine-induced relaxation of aortic rings in a concentration-dependent manner. The inhibitory effects by arsenic were also observed in the relaxation induced by sodium nitroprusside, a NO-donor. Consistent with these findings, the cGMP levels stimulated by acetylcholine in blood vessels were reduced significantly by arsenite treatment. In addition, higher concentration of arsenite decreased the relaxation by 8-Br-cGMP, a cGMP analog, in aortic rings without endothelium. These in vitro results indicated that arsenite was capable of suppressing acetylcholine-induced relaxation in blood vessels by inhibiting production of nitric oxide in endothelial cells and by impairing the relaxation machinary in smooth muscle cells. In vivo studies revealed that the reduction of blood pressure by acetylcholine infusion was significantly suppressed after arsenite was administered intravenously to rats. These data suggest that vasomotor tone impaired by arsenite exposure may be one of the contributing factors in development of cardiovascular disease.

[PA3-14] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Evidence of TCDD-like activities in crude and fractionated extracts of PM 2.5 diesel particle material using EROD-microbioassay.

Jang HyoungSeok°, Han KyuTae, Oh SeungMin, Chung KyuHyuck

College of Pharmacy, SungKyun University 300, suwon, Kyungkido 440-746, Korea

Diesel motors exhaust particulate material, which is known to be mutagenic, has caused heavy air pollution. PM 2.5 diesel exhaust of vehicle was collected using a high-volume sample equipped with a cascade impact. The crude extract was fractionated according to EPA recommended procedure into seven fractions by acid-base partitioning and silica gel column chromatography. We examined Ah receptor-mediated activities of fractionated samples using EROD microbioassay in H4IIE rat hepatoma cell line and HepG2 human hepatoma cell line. EROD microbioassay was conducted to determine cytochrome P4501A activity in environmental samples, and the TCDD equivalent concentration(TEQ) was calculated for the quantitative assessment. The biological TEQ was calculated by comparing the concentration response curve of the sample with those of the TCDD calibration curve. In the results, we confirmed that a large quantity of TCDD-like components was presented in PM 2.5 diesel exhaust particulate materials. Higher potency was observed in crude extract and nonpolar fraction. Since, it is reported that aliphatic and aromatic compounds such as chlorinated hydrocarbons, PAH and their alkylderivatives are contained nonpolar fraction, we presume that these chemicals may relate to TCDD-like activities.

[PA3-15] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Inorganic Arsenic Increases Vasoconstriction through Calcium-Sensitization in Vascular Smooth Muscles

Lee MY°, Lee YH*, Bae OK, Chung JH

College of Pharmacy, Seoul National University, Seoul 151-742, and *College of Medicine, Yonsei University, Seoul, 120-752, Korea

Chronic exposure of arsenic is well known to be the cause of cardiovascular disease such as hypertension. In order to investigate the effect of arsenic on blood vessels, we examined whether arsenic affected agonist-induced contraction of aortic rings in isolated organ bath system. Treatment with arsenite increased vasoconstriction induced by phenylephrine or serotonin in a concentration-dependent manner. Similar effects were also shown in the aortic rings without endothelium, suggesting that vascular smooth muscle played a key role in enhanced vasoconstriction induced by arsenite. Arsenite is the most potent form among arsenic species tested. These alterations were well correlated with myosin light chain (MLC) phosphorylation induced by arsenite in smooth muscles. Direct calcium measurement using fura-2 dye in aortic rings revealed that arsenite enhanced contraction by high K+ without further increase in intracellular calcium levels. Calcium-sensitization of contractile machinery, therefore, may contribute to the enhanced vasoconstriction by arsenite. Consistent with these in vitro results, intravenous administration of 1.0 mg/kg arsenite augmented blood pressure increase induced by phenylephrine in conscious rats. These results suggest that arsenite increases agonist-induced vasoconstriction mediated by MLC phosphorylation and calcium-sensitization in smooth muscles was one of the key mechanisms for the arsenite-induced hypercontraction in blood vessels.

[PA3-16] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Evaluation of genotoxic potentials in diesel exhaust particulate matter with the Ames test, the comet assay and the micronucleus assay

Kim SoungHo°, Lee DoHan, Han KyuTae, Oh SeungMin, Chung KyuHyuck

College of Pharmacy, SungKyun University 300, suwon, Kyungkido 440-746, Korea

This research was designed to examine the presence of mutagenic/carcinogenic compounds in airborne pollutants in diesel particulate matter using an integrated biological approach. Respirable air borne particulate matter (PM2.5: <2.5mm) was collected from diesel engine exhaust using a high-volume sampler equipped with a cascade impactor. Particulate oganic matter was extracted by the dichloromethane/sonication method and the crude extract was fractionated according to EPA recommended procedure into seven fractions by acid-base partitioning and silica gel column chromatography.There are several methods for assessing DNA-damage at the DNA and chromosomal level.
The comet assay and in vitro MN test are newly designed genotoxicity methods.In this study, we assessed genotoxic potentials of diesel exhaust particulate matter with the Ames test, the comet assay and in vitro MN test.This test seems to be sensitive to genotoxins as found in many previous research on air pollution and a promising test for monitoring airborne genotoxins in environments.The results showed the applicability of this genotoxicity tests which reveal different genetic end-points (DNA-damage, point mutation and micronuclei) detected the presence of genotoxins.Positive results were observed in some of fractions using the in vitro MN test and the comet assay . A statistically significant increase in micronuclei was found in aromatic and slightly polar fraction of the revealing the presence of unknown genotoxic compounds .
The results indicated that diesel exhaust particulate matter induced DNA damage in DNA and chromosome levels. Therefore, genotoxic potentials are present in diesel exhaust particulate matter.

[PA3-17] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Estrogenic/antiestrogenic potencies in crude and fractionated extracts of diesel exhaust particulate matter(PM) on human breast cancer cell

Ryu byungTaek°, Kim YunHee, Han kyuTae, Oh SeungMin, Chung KyuHyuck

College of Pharmacy, SungKyun University 300, suwon, Kyungkido 440-746, Korea