compounds (1,2-Dimethyl-3-phenylaziridine, amphetamine oxime, ephedrine, N-formylmethamphetamine, N-acetylmethamphetamine, acetylephedrine, 3,4-dimethyl-5-phenyl-2-oxazolidone, methamphetamine dimer) are identified impurities in illicit methamphetamine and the identity of the impurity is conformed synthesis. Identification of other impurities found on the chromatrogram is under investigation. These impurities revealed that most of the seized methamphetamine in Korea was synthesized from ephedrine as a starting material.

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MODULATION OF THE ACTIVITY OF PRO-INFLAMMATORY ENZYMES, COX-2 AND iNOS, BY CHRYSIN DERIVATIVES

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Chrysin, a natural flavone compound contained in plants, has anti-inflammatory activity. Its anti-inflammatory effect has been previously explained in part by the suppression of promoter activities of inducible pro-inflammatory enzymes (cyclooxygenase-2 (COX-2) and inducible nitrogen synthase (iNOS)). Nitrate production triggered by the activation of lipopolysaccharides (LPS) was most highly suppressed by the treatment of chrysin, followed by 5-hydroxy-7-methoxyflavone (Ch-2), 5,7-diacetylflavone (Ch-4) in cultured Raw 264.7 cells. Here we tested the inhibitory activity of chrysin derivatives on COX-2 and iNOS enzymes. Interestingly COX-2 enzyme was strongly inhibited by Ch-2 (IC50 = 2.7 mM) but not by other derivatives. Furthermore, the inhibition of COX enzyme by Ch-4 was selective on COX-2 isoenzyme over COX-1. The three-dimensional interaction models of Ch-4 complexing with COX-2 showed comparatively good fit into the topology of the binding pocket. There was a hydrogen bond between oxygen of ketone group of the 7-positon of Ch-4 and the hydroxyl group of Tyr355. Docked conformation of Ch-4 into V523I mutant of COX-2 indicated that Ile523 of COX-1 might contribute to the selectivity of COX-2/COX-1. Ch-4 showed no effect on iNOS activity. Chrysin and Ch-2 weakly inhibited iNOS enzyme activity in hemoglobin assay. However, the underlying mechanisms of the inhibition of iNOS by chrysin are not clear.

[PD4-28] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

In vitro metabolism of a new protective agent, KR-31543 in human liver microsomes

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The purpose of this paper was to identify the metabolic pathway of a new neuroprotective agent, KR-31543 for ischemia-reperfusion damage in human liver microsomes and characterize cytochrome P450 (CYP) enzymes involved in the in vitro metabolism of KR-31543. KR-31543 generates two metabolites in human liver microsomes: M1, N-(4-chlorophenyl)-N-(2-methyl-2H-tetrazol-5-ylmethyl)amine and M2, hydroxy-KR-31543. From a combination of chemical inhibition, immunoinhibition, correlation analysis in human liver microsomes and metabolism by expressed recombinant CYP enzymes, KR-31543 is metabolized predominantly by CYP3A4 and is mainly converted to M1, N-(4-chlorophenyl)-N-(2-methyl-2H-tetrazol-5-ylmethyl)amine. KR-31543 was found to be a potent inhibitor of human CYP2D6 and 3A4 in human liver