[PE2-5] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

In vitro metabolism of YH1885 by human liver microsomes and recombinant human cytochrome P450s

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YH1885,[5,6-dimethyl-2-(4-fluorophenylamino)-4-(1-methyl-1,2,3,4-tetrahydroisoquinolin-2-yl) pyrimidine hydrochloride], is a novel acid pump antagonist being developed by Yuhan Research Center as an antiulcer agent. To evaluate the metabolic profile and identify cytochrome P450(CYP) isoforms involved in the metabolism of YH1885 in human, we investigated the hepatic metabolism of YH1885 by using human liver microsomes and recombinant human cytochrome P450s. We also investigated the interaction of YH1885 with specific markers of CYP isoforms.
The formation of metabolites was characterized by KM and Vmax. The high KM values of major metabolites (≥ 219μM) suggested relatively low affinity of YH1885 to cytochrome P450. Therefore, YH1885 is likely to be hardly metabolized in human liver. The formation of major metabolites was mainly mediated by CYP3A4 and CYP1A2. The Ki values for caffeine 3-demethylation (CYP1A2) and testosterone 6β-hydroxyation (3A4) were much higher than the presumed concentration of YH1885 in clinical studies. Therefore, it is expected that YH1885 would cause little interaction with other drugs.
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[PE2-6] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Pharmacokinetics of BR-A657 in rats ; A New angiotensin II receptor antagonist

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BR-A657 is analogue of losartan potassium which is orally active non-peptide A II receptor antagonist. In this study BR-A657 was determined by high-performance liquid chromatography in rat plasma with ultraviolet detection and its pharmacokinetic parameter in i.v. administration was calculated. Plasma samples were extracted by methyl tert.-butyl ether in pH 3 then back-extracted by 0.05 M NaOH Samples were analyzed by reversed-phase HPLC system using μBondapak C18 column with ultraviolet detection at 261 nm. Detection limit was 20nM. 50 mg/kg of potassium salt and base form of BR-A657 was orally administered to rats. Both form of BR-A657 were rapidly absorbed and Cmax was 20 minutes. But bioavailability of potassium salt form was better than that of base form. In 1 mg/kg intravenous administration to rats, plasma concentration-time profile was best characterized by 2-compartment model. T1/2α and T1/2β were 0.02±0.01 hr, 0.24±0.10 respectively. Clearance, volume of distribution, and AUC were 5.75±1.18 L/kg/hr, 0.37L/kg/hr, 179.03±37.74 ng·hr/ml, respectively

[PE2-7] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Pharmacokinetic study of CWJ-a-5

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