dependent

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Dimethyl-4, 4'-dimethoxy-5, 6,5', 6'-dimethylenedioxybiphenyl-2, 2'-dicarboxylate (DDB), an anti-viral hepatitis agent, has been identified as a selective CYP3A4 inhibitor through the formation of stable MI-P450 complex.
In this study, the inhibitory effects of DDB on CYP3A4 activity were investigated using a series of CYP3A4-specific substrate to clarify potential drug-drug interactions. The inhibitory potency of DDB was depending on the type of substrates in human liver microsomes.Testosterone hydroxylation and nifedipine oxidation were highly inhibited with IC_{50} value of 0.35μM and 4.04μM, respectively. However metabolism of midazolam, erythromycin, and terfenadine in human liver microsomes were less inhibited by DDB with 10-100 times higher IC_{50} values compared to testosterone 6β-hydroxylation. These results indicated that interaction between drugs metabolized by CYP3A4 are substrate-dependent and these phenomena can be explained by the existence multiple substrate-binding site in CYP3A4.

[PA1-10] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Mechanism of Hypoglycemic Effect of (R)-JG-381 in Rat

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The present study was undertaken to investigate hypoglycemic mechanism of (R)-JG-381, a new oxirane-2-carboxylate derivative. Diabetes mellitus was produced for intravenous injection of streptozotocin (45 mg/kg b.wt.). After 1 week of administration of streptozotocin, the rats then received vehicle (0.5% CMC) or (R)-JG-381(10, 40 mg/kg b.wt./day) orally for 4 weeks. We have determined blood glucose, the lipid metabolites such as b-hydroxybutyrate, triglyceride and cholesterol concentrations in blood and carnitine palmitoyl transferase activity, triglyceride and cholesterol content in liver. In streptozotocin-treated rat, blood glucose levels were significantly increased and the level of lipid metabolites, b-hydroxybutyrate, triglyceride and cholesterol in blood were also increased. (R)-JG-381 decreased the elevated glucose level. The increase in b-hydroxybutyrate, triglyceride and cholesterol concentrations in blood was suppressed by (R)-JG-381 treatment. Our findings suggest that (R)-JG-381 decreases lipid oxidation in diabetic rats.

[PA1-11] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

The influences of ELF magnetic fields on hyperalgesia and convulsion in rat

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The effect of extremely low frequency (ELF, 60Hz) magnetic fields (MFs) on hyperalgesia and convulsion was studied using hot plate tests and convulsion tests in rats. In addition, we measured GABA concentration using HPLC-ECD in rat brain. In hot plate tests, MFs or diazepam (0.5 μg, i.c.v.) had hyperalgesic effects. These effects were blocked by flumazenil (1.5 mg/kg, i.p. ; benzodiazepine receptor antagonist). Flumazenil also inhibited hyperalgesia induced by MFs and diazepam. This indicate that MFs-induced hyperalgesia may be mediated through activation of benzodiazepine receptor. MFs-induced hyperalgesia was not changed by bicuculline (0.1 μg,

i.c.v. ; $GABA_A$ antagonist) or phaclofen (10 μg, i.c.v. ; $GABA_B$ antagonist). In convulsion tests, MFs strengthened convulsion induced by bicuculline (0.3, 1, 3 μg, i.c.v.) in induction and duration time. MFs decreased the concentration of GABA in the hippocampus. MFs and bicuculline (1μg, i.c.v.) decreased the concentration of GABA than bicuculline alone treatment in the cortex, hippocampus and cerebellum. The present study suggests that MFs participate in hyperalgesia or convulsion which is mediated by benzodiazepine or GABA receptor, respectively.

[PA1-12] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

PK-PD modeling of antiplatelet and cardiovascular effect of cilostazol in humans

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The rationale for PK-PD modeling is to link PK and PD in order to establish and evaluate dose-concentration-response relationships and subsequently describe and predict the effect-time courses resulting from a drug dose. Cilostazol, PDE III inhibitor, inhibit platelet aggregation and increase cardiovascular function such as heart rate, myocardial contractile force, coronary blood flow, and ventricular automaticity in a dose-related fashion. The relationships between plasma concentration of cilostazol and its inhibitory effect on platelet aggregation and cardiovascular effect after single oral administration 100mg of cilostazol in healthy humans were analyzed using a PK-PD model. Plasma levels of cilostazol were measured by HPLC. Pharmacokinetic and pharmacodynamic parameters were estimated using the ADAPT II programs by weighted least squared method. Pharmacokinetics of cilostazol was explained by two compartment model with first-order absorbtion for the oral bolus route. Direct and indirect response models were applied for antiplatelet and cardiovascular effect of cilostazol.

[PA1-13] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Effect of Chondroitin Sulfate and Phelinus Linteus mushroom on melanin and skin-whitening

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This study was conducted to develop a new biomaterial to be used for skin whitening.
The melanin elimination effect of chondroitin sulfate and phelinus linteus mushroom in rabbit back skin were evaluated. Rabbit dorsum was exposed to chronic UV irradiation(320nm) once daily for 30 days after initial melanin injection (100mg/kg). And then, chondroitin sulfate and phelinus linteus mushroom at dose of 0.7g for 30days were applied on the zone. The dorsal skin was histologically examined. Furthermore, we investigated free-radical extinction effect, antioxidation and tyrosinase activity inhibition effects.
The histological study indicated that chondroitin sulfate and phelinus linteus mushroom decreasd melanine pigment significantly. As a result, chondroitin sulfate and phelinus linteus mushroom have a remarkable effect on the skin whitening by melanin elimination.

[PA1-14] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Studies on the antioxidative effect of Polygoni Raidx