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,