P-2

Drug interaction between nicardipine and pioglitazone

Yong-Ji Piao and Jun Shik Choi

College of Pharmacy, Chosun University, Gwangju 501-759, Korea

Pioglitazone, a thiazolidinedione antidiabetic drug, inhibits cytochrome P450(CYP) 2C8 and CYP 3A4 enzymes in vitro. This study investigated the effect of pioglitazone on the bioavailability of orally and intravenously administered nicardipine, which is a substrate for P-gp and CYP 3A in rats. A single oral (12 mg/kg) or intravenous (4 mg/kg) dose of nicardipine was administered to rats alone or with oral dose of pioglitazone (0.3 or 1.0 mg/kg) administration. Compared to the oral control group, the presence of pioglitazone significantly ($p<0.01$) increased the area under the plasma concentration-time curve (AUC) of nicardipine by 115-150% and the peak concentration (C_{max}) by 97-107%, and significantly ($p<0.01$) decreased the total plasma clearance (CL/F) of nicardipine by 49.7-56.6%. The enhanced oral bioavailability of nicardipine might be due to the decreased efflux and metabolism of nicardipine in the intestine. The presence of 1.0 mg/kg of pioglitazone also altered the pharmacokinetics of i.v. administered nicardipine. Compared to the i.v. control, the presence of 1.0 mg/kg of pioglitazone significantly ($p<0.05$) increased the AUC of nicardipine by 38.9%.

Our results indicate that pioglitazonesignificantly enhanced oral bioavailability of nicardipine in rats. Drug interactions should be concerned in the clinical setting when nicardipine is coadministrated with pioglitazone.

Key words: nicardipine, pioglitazone, pharmacokinetic, rats