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Effect of nonalcoholic fatty liver disease on CYP2B1-mediated metabolism in rats

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Nonalcoholic fatty liver disease (NAFLD) is defined as a condition that excessive fat is accumulated in hepatocytes without substantial alcohol intake, and refers to hepatic pathologies ranging from simple fatty liver (SFL; steatosis) to nonalcoholic steatohepatitis (NASH), fibrosis and cirrhosis, that may progress to hepatocellular carcinoma. These liver disease states may affect the activity and expression levels of drug-metabolizing enzymes, potentially resulting in an alteration in the pharmacokinetics, therapeutic efficacy and safety of drugs. This study investigated the hepatic cytochrome P450 (CYP) 2B1-modulating effect of a specific NAFLD state in dietary rat models. Sprague–Dawley rats were given a methionine/choline-deficient (MCD) or high-fat (HF) diet for eight weeks to induce NASH and SFL, respectively. The induction of these disease states was confirmed by Plasma Chemistry and Liver Histological Analysis. Both the protein and mRNA level of hepatic CYP2B1 was considerably reduced in MCD diet-fed rats, however, it tended to be similar between the HF diet-fed and control rats. Consistently, the enzyme-kinetic and pharmacokinetic parameters for CYP2B1-mediated bupropion metabolism were considerably reduced in MCD diet-fed rats, however, it tended to be similar between the HF diet-fed and control rats. These results may promote a better understanding about the influence of NAFLD on CYP2B1-mediated metabolism, which could have important implications for the safety and pharmacokinetics of CYP2Bs substrate drugs in patients with NAFLD.

Biography

Dae-Duk Kim has completed his PhD in 1995 from Rutgers University - The State University of New Jersey in the USA and worked as a Post-doctoral Fellow at the University of Washington in Seattle. He was a Faculty Member of the College of Pharmacy at Pusan National University until he transferred to his current position at Seoul National University in 2003. He has published more than 180 papers in peer-reviewed international journals, and has served as the Editor-in-Chief of the *Journal of the Pharmaceutical Investigation*. His research focuses on the optimization of therapeutic systems to maximize drug efficacy and minimize toxicity. He has developed diverse drug delivery systems that can control absorption and sustain drug action.

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