P-32

THE EFFECT OF COPROPHAGY ON THE EXPRESSION OF HEPATIC CYP2E1 DURING STARVATION

Hye Chin Chung, Sang Hyun Sung, Jin Soo Kim, Young Choong Kim and Sang Geon Kim*

College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul National University

Starvation stimulates multiple signaling pathways, which lead to extensive metabolic alterations Starvation potentiates the hepatotoxicity of a variety of small molecules including chlorinated hydrocarbons and nitrosamines through the induction of CYP2E1. A change in CYP2E1 expression during starvation may also alter the pharmacokinetic profiles of xenobiotics. Northern blot and Western blot analyses revealed that hepatic CYP2E1 was not induced during starvation in rats placed in metabolic or wire bottom cages in contrast to the induction of CYP2E1 in animals housed in solid bottom cages. We studied the effect of coprophagy on the expression of hepatic CYP2E1 during starvation. The extent of coprophagy was 24% in fed rats. Fecal matter of starving rats was reduced to 14% of control and starving rats re-ingested ~1.6 g of feces per day. The effect of fecal matter on CYP2E1 expression (i.e. 1.6 g/kg/day, for 3 days) was assessed in fed or starving rats. Starving rats gavaged with fecal matter for 3 days resulted in a 3.5-fold increase in the level of CYP2E1 mRNA, while fed rats gavaged with feces failed to show an increase in the mRNA. The increase in the CYP2E1 mRNA level accompanied the induction of CYP2E1. Starving rats gavaged with methanol extract of feces (500 mg/kg/day, for 3 days) showed a 3.3-fold increase in CYP2E1 mRNA level in the liver. In conclusion, starvation failed to induce CYP2E1 protein and mRNA levels, and re-ingestion of fecal matter contributed to CYP2E1 induction in starving animals, but not in fed animals. These results provide evidence that CYP2E1 is not induced by starvation without coprophagy, raising the contention that the mechanistic basis for CYP2E1 induction by starvation should be re-evaluated.