P-56

ALTERATIONS IN HEPATIC GSH SYNTHESIS INDUCED BY PROPARGYLGLYCINE IN MICE

Sang K. Kim, Sung Y. Kim, Jung M. Seo, and Young C. Kim

College of Pharmacy, Seoul National University, Seoul 151-742, Korea

Effects of propargylglycine (PPG) treatment on the hepatic glutathione (GSH) synthesis were examined in adult male ICR mice. Administration of PPG (200 mole/kg, ip) to mice resulted in a complete inhibition of the hepatic cystathionine γ-lyase (CγL) activity measured in cytosol fraction for 40 hr after the treatment. A single injection of PPG rapidly reduced the hepatic GSH levels, which appeared to be sustained at least for 40 hr. The GSH concentration in plasma was significantly decreased for 20 hr, but recovered to the control level in 40 hr. Renal GSH levels did not appeared to be changed by PPG treatment. The cysteine concentrations in liver, kidney and plasma were also decreased by PPG. The effect of PPG pretreatment was examined in mice challenged with methionine (1 mmole/kg, po), the sulfur donor in the transsulfuration pathway. Methionine administration elevated S-adenosylmethionine (SAM) and GSH concentrations in liver significantly when measured 3 hr following the treatment. In PPG pretreated mice the hepatic SAM level was increased, however, elevation of GSH by methionine was inhibited completely suggesting that the supply of cysteine from the methionine cycle for GSH synthesis in liver was blocked by PPG. The results show that generation of cysteine in the transsulfuration pathway has a critical role in the hepatic synthesis of GSH, and PPG can be used as an effective tool for study of sulfur-containing amino acid metabolism in liver.