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INHIBITION OF HEPATIC FIBROGENESIS INDUCED BY NITROSODIMETHYLAMINE IN RATS PRETREATED WITH BETAINE

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Effects of betaine intake on hepatic fibrogenesis were examined in adult male SD rats treated with nitrosodimethylamine (DMN; 10 $\mu\ell$/kg/day, ip) 3 days a week for 4 weeks. From two weeks prior to initiation of DMN treatment until sacrifice rats were provided with drinking water containing 1 % betaine. DMN treatment at this dosage regimen resulted in hepatic fibrosis as determined by changes in hepatic 4-hydroxyproline contents and serum biochemical parameters, such as alanine aminotransferase, aspartate aminotransferase, total bilirubin and plasma protein contents. Hepatic microsomal enzyme activities were also reduced in rats treated with DMN. Betaine intake significantly decreased the changes induced by DMN, which was further supported by the results of histopathological examination of rat liver. DMN treatment also elevated hepatic concentration of malondialdehyde measured by HPLC analysis, which was completely blocked by betaine. In liver of rats treated with DMN, S-adenosylmethionine level was decreased but cysteine, taurine, glutathione disulfide and homocysteine levels were all increased. Consistent changes in the activities of critical enzymes involved in the transsulfuration pathway were also observed. Betaine intake inhibited all the changes in the metabolic intermediates/products and enzyme activities induced by DMN. It is suggested that antifibrotic activity of betaine could be associated with its potential for maintaining homeostasis of hepatic sulfur-containing amino acid metabolism.

keyword : betaine, nitrosodimethylamine, S-amnio acid, glutathione, fibrosis