



Changes in the Enzyme Activity of CYP450 in Rats with Liver Cirrhosis Induced by Thioacetamide

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SUMMARY. To study the changes in the enzyme activity of cytochromes P450 (CYP450) in rats with liver cirrhosis induced by thioacetamide (TAA), three probe drugs (phenacetin, tolbutamide and omeprazole) were simultaneously given to Sprague-Dawley rats which were randomly divided into 2 initial groups: the control (n = 6) and cirrhotic (n = 10) rats. Rats were given TAA in their drinking water at a concentration of 0.03% for 5 consecutive weeks and then 0.04% for the next 5 consecutive weeks throughout the establishment of cirrhosis. At the end of treatment, blood was collected for biochemical tests of serum alanine aminotransferase (ALT) and liver tissues were processed for histological examination with HE staining. The plasma concentrations of three probes were measured by LC-MS. The result showed that the levels of ALT (132.22% increase) were significantly higher in cirrhotic rats than the controls, and fully developed cirrhotic nodules surrounded by thick fibrous septa. There was obvious difference in plasma concentrations and corresponding pharmacokinetic parameters of phenacetin, tolbutamide, and omeprazole between two groups. In cirrhotic rats, the AUC of phenacetin and omeprazole was significantly greater (418.64 and 133.98% increase, respectively), C_{max} was significantly higher (107.63 and 405.38% increase, respectively), the terminal half-life (t_{1/2}) was significantly shorter (72.15 and 83.88% decrease, respectively) and CL was significantly slower (80.42 and 57.09% decrease, respectively) than controls. In conclusion, the enzyme activity of CYP2C19 and CYP1A2 decreased in cirrhotic rats induced by TAA.

KEY WORDS: CYP450, Liver cirrhosis, Pharmacokinetic, Rat, Thioacetamide.

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