

derivatives. Five sets of primers were designed and one set was selected for RT-PCR. We have found that QIAamp viral RNA isolation kit was the most efficient extraction kit for these systems when several PCR conditions such as annealing temperature, reverse transcription temperature and MgCl₂ concentration, etc. were optimized. The sensitivity was calculated to be 100 IU/ml and HCV RNA negative plasma pools showed negative. Both in-house method and COBAS amplicor HCV 2.0 showed positive for window period samples. ELISA-confirmed positive samples also provided 80.6% positive rate. With a spiking of HCV to albumin, immunoglobulins and coagulation factors, the in-house method can detect up to 100IU/ml. Meanwhile, COBAS amplicor HCV 2.0 afforded a lower sensitivity in high concentrated intramuscular immunoglobulins to 500IU/ml. Results of our investigation confirm that the in-house NAT appears to be a highly sensitive and specific method, which is reliable for plasma as well as for plasma-derived medicinal products.

[PB2-6] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Alteration of Hepatic Drug Metabolizing Function after Traumatic Injury

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The aim of present study was to investigate effects of blunt trauma on alterations in cytochrome P-450 (CYP)-dependent drug metabolizing function and to determine the role of Kupffer cells in the hepatocellular dysfunction. Rats underwent closed femur fracture (FFx) with associated soft-tissue injury under anesthesia. Control animals received only anesthesia. To deplete Kupffer cells in vivo, gadolinium chloride (GdCl₃) was injected intravenously via the tail vein at 7.5 mg/kg body wt. 1 and 2 days before surgery. At 72 h after FFx, serum alanine aminotransferase (ALT) activity was increased, and this increase was attenuated by GdCl₃ pretreatment. Serum aspartate aminotransferase (AST) and lipid peroxidation levels were not changed by FFx trauma. Hepatic microsomal CYP content and aniline *p*-hydroxylase (CYP 2E1) activity were significantly decreased, which were not prevented by GdCl₃. The level of CYP 2B1 activity was decreased by Kupffer cell inactivation, but not by FFx. There were no significant differences in the activities of CYP 1A1, CYP 1A2 and NADPH-CYP reductase among all experimental groups. Our findings suggest that FFx trauma causes mild alteration of hepatic CYP-dependent drug metabolism and Kupffer cells are not essential for the initiation of such injury.

[PB2-7] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Effect of Trolox C on CYP450 Isozymes Activity and Expression in Hepatic Ischemia/Reperfusion

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The present study was done to determine the effect of trolox C, a hydrophilic analogue of vitamin E, on alteration in cytochrome P-450 (CYP)-dependent drug metabolism during ischemia and reperfusion. Rats were subjected to 60 min of hepatic ischemia and 5 h of reperfusion. Rats were treated intravenously with trolox C (2.5 mg/kg) or vehicle (PBS, pH 7.4), 5 min before reperfusion. Serum alanine aminotransferase and lipid peroxidation levels were markedly increased after ischemia and reperfusion. This increase was significantly suppressed by trolox C. Cytochrome P-450 content and NADPH-cytochrome P-450 reductase activity were decreased by ischemia/reperfusion, and restored by trolox C. Furthermore trolox C significantly increased NADPH-cytochrome P-450 reductase protein expression. There were no significant differences in ethoxyresorufin *O*-deethylase (CYP 1A1) and methoxyresorufin *O*-demethylase (CYP 1A2) activities among all experimental groups. While pentoxyresorufin *O*-dealkylase (CYP 2B1) activity was decreased, aniline *p*-hydroxylase (CYP 2E1) activity and its protein expression was increased by ischemia and reperfusion, which were prevented by trolox C. Our findings suggest that ischemia and reperfusion induces hepatic microsomal dysfunction by increasing lipid peroxidation, and trolox C ameliorates this change through its free radical scavenging activity.

[PB2-8] [10/17/2002 (Thr) 13:30 - 16:30 / Hall C]

Kupffer Cells Are Responsible for Producing Hepatic Microsomal Drug Metabolizing Dysfunction during Trauma and Sepsis