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Blood and Liver Acetaldehyde Concentration in Rats Following Acetaldehyde Inhalation and Intravenous and Intragastric Ethanol Administration

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Ethanol is metabolized to acetaldehyde, a highly reactive product of ethanol oxidation. Ethanol might be blended with gasoline and used as a fuel in the future; biohazard of acetaldehyde inhalation must be discussed. Recent improvements in our ability to measure acetaldehyde levels in blood and various tissues have made the assessment of acetaldehyde's role in alcoholic organ intoxication possible. Blood and liver acetaldehyde concentrations in rats were reported as being linearly correlated following intragastric ethanol administration (Eriksson et al. 1977). Acetaldehyde was administered by inhalation to study its toxicity (Nishino et al. 1982). However, liver concentrations following the inhalation was not investigated. The present communication describes the relationship between blood and liver acetaldehyde concentrations in rats following acetaldehyde inhalation and different routes of ethanol administration.

MATERIALS AND METHODS

Male Sprague-Dawley rats, weighing 230 to 280 g each, were used throughout the study. Intragastric and intravenous administration of ethanol used doses of 3 to 6 g and 0.3 to 1.0 g per kg body weight, respectively. Acetaldehyde levels were determined 1 hr following the administration. Acetaldehyde inhalation was accomplished by exposing rats to acetaldehyde gas at a flow rate of 1 l/min for 1 hr by passing air through 400 ml of freshly-prepared 0.5 to 3.0% aqueous acetaldehyde solution in a sealed box (53 X 42 X 32 cm). Acetaldehyde levels in the air in the box were kept 9 mg/l to 1 g/l. Immediately after discontinuation of inhalation, rats were exsanguinated from the carotid artery, to prevent tissue contamination by blood acetaldehyde, without anesthesia and the livers removed.

Arterial blood and liver acetaldehyde concentrations were determined by a head-space gas chromatographic method (Watanabe et al. 1985). Average recovery of acetaldehyde was found to be 100.1%.

RESULTS AND DISCUSSION

Blood and liver acetaldehyde concentrations were well-correlated over the physiological range (Fig. 1). Acetaldehyde inhalation resulted in blood concentrations very much higher than liver levels; even at a blood level greater than 10 µg/ml, the liver level was less than 2.5 µg/g. Correlations between blood and liver acetaldehyde levels were essentially similar following intragastric and intravenous ethanol administration; liver contents exceeded blood levels. With blood acetaldehyde concentrations higher than 1 µg/ml the liver levels following intragastric administration were slightly higher than following intravenous injection. The relation between blood and liver acetaldehyde levels following acetaldehyde inhalation was completely different from those following ethanol administration. This was probably due to quick absorption of acetaldehyde from the lung and its rapid oxidation in the peripheral tissues including the lung which possess aldehyde dehydrogenase (Deitrich 1966). Following acetaldehyde inhalation, levels in arterial blood were higher than in peripheral venous blood (data not shown). Thus, the bulk of acetaldehyde was metabolized extrahepatically, with only a minor amount reaching the liver.

Oxidation of ethanol to acetaldehyde by alcohol dehydrogenase occurs mainly in the liver; here aldehyde dehydrogenase activity is also high. The higher liver levels following intragastric ethanol administration than after intravenous injection probably resulted from total liver presentation of ethanol via portal vein first passage in the former. Disappearance of ethanol from the blood was very rapid following the intravenous administration of smaller doses of ethanol. The role of exhaled acetaldehyde in extrahepatic acetaldehyde elimination, and different determinations of erythrocyte and plasma acetaldehyde are currently under study.

Comparative experimental data are not available for man. Blood acetaldehyde concentrations are higher in chronic alcoholics than non-alcoholics after intragastric administration of a standard amount of ethanol (Korsten et al. 1975). The reasons for this are not

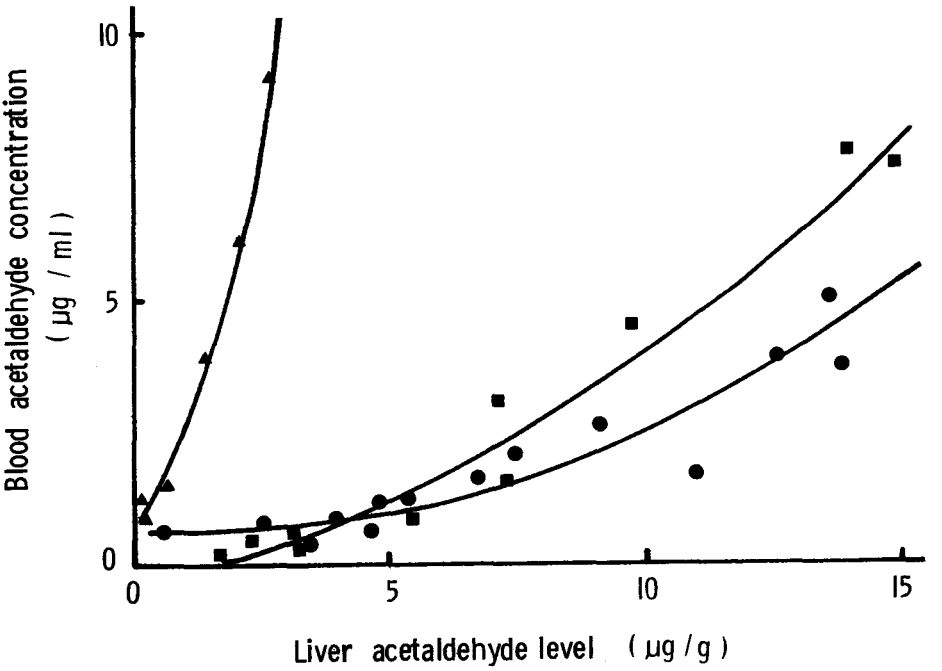

Figure 1. Relationship between arterial and liver acetaldehyde concentrations following acetaldehyde inhalation (▲, $Y = 0.039X^2 + 1.133X + 12.882$, No. of rats = 6), and intravenous (●, $Y = 0.001X^2 + 0.033X + 13.993$, No. of rats = 13) and intragastric (■, $Y = 0.001X^2 + 0.211X - 9.345$, No. of rats = 10) ethanol administration to rats.

known. However, measured blood levels in these cases can be employed to approximate the liver acetaldehyde levels, analogous to the present study.

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