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EFFECT OF p-TERT-BUTYLPHENYL TRANS-4-GUANIDINOMETHYL CYCLOHEXANE CARBOXYLATE HYDROCHLORIDE (NCO-650) ON DRUG-METABOLIZING ENZYMES AND PINE STRUCTURE IN RAT LIVER: Sadao NAKAYAMA, Takako KASAHARA and Hajime YASUHARA (Dept. of Pharmacology, School of Medicine, Showa University. Hatanodai, Shinagawa-ku Tokyo 142)

It is known that the administration of p-tert-butylphenyl trans-4-guanidinomethyl cyclohexane carboxylate hydrochloride (NCO-650) leads to various biomembrane effects in animal, including an inhibition of release of chemical mediator from mast cell in rats and of hypotonic hemolysis on rat erythrocytes or enzyme leakage from rat isolated hepatocytes. In the present report, effect of NCO-650 on the liver in rats were investigated by the determination of drug-metabolizing enzyme activities and morphological changes in liver tissue detected using electron microscopy. A single administration of NCO-650 (10, 100 and 1000mg/kg, p.o.) induced an apparent increase in liver drug-metabolizing enzymes. The elevation of aminopyrine demethylase activity and increased in microsomal cytochrome P-450 and cytochrome b$_5$ content were seen with the administration of NCO-650. The lipid peroxide formation increased by the administration of NCO-650. NCO-650 caused the morphological changes of liver fine structure such as disarrangement of rough endoplasmic reticulum, detachment of ribosome, increase in smooth endoplasmic reticulum and swelling of mitochondria. In these results, effect of NCO-650 on the liver were not apparently a functional or toxic responses. The effect of NCO-650 on the liver may have relation to the membrane effect.

MITOCHONDRIAL ALDEHYDE DEHYDROGENASE ACTIVITIES AFTER ADMINISTRATION OF ETHANOL IN RATS: Yoshikazu AOKI, Sumiyoshi OHTSUKA, Yumi KUSHIRO, Masae KOBAYASHI, Tomoyo FUKUCHI, Reiko WATANABE and Hajime ITOH (Dept. of Clinical Chemistry, Kitasato University School of Hygienic Sciences. Sagamihara, Kanagawa Pref.)

Aldehyde dehydrogenase (ALDH) isoenzyme activities in liver mitochondria were examined in Fischer rats given long term and a single administration of ethanol.

In long term ethanol administration for seven months, both Low-Km ALDH activity in matrix and High-Km ALDH activity in outer membrane were increased to 2-3 times of control value. But aspartate and alanine aminotransferases, alkaline phosphatase and gamma glutamyl transpeptidase activities, and cholesterol, triglyceride and protein contents in liver and serum were not changed in these conditions.

In a single administration of ethanol (5g/kg b.w.), High-Km ALDH and Low-Km ALDH activities were increased to 21 and 4.4 times of control value, respectively.

Consequently, it seemed that Low-Km ALDH in matrix as well as High-Km ALDH in outer membrane was activated while mitochondria was continuously exposed low level acetaldehyde. On the other hand, it was suggested that High-Km ALDH was related to acetaldehyde metabolism, as acetaldehyde concentration was significantly elevated in liver mitochondria by a single administration of ethanol.

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