

## DOSE-EFFECT- AND DOSE-RESPONSE-RELATIONSHIPS IN RATS PERORALLY ADMINISTERED WITH ETHANOL IN LIQUID DIET.

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A subchronic experiment with ethanol was designed to evaluate the highest test dose to be used in a subsequent carcinogenicity bioassay. Sprague-Dawley rats were given 1, 2, 3, 4, 5, 10, 15, and 25% w/w ethanol in semisynthetic liquid diet for 13 weeks in two experiments. In one experiment glucose and pure diet was used as controls. Body weights were developing equally between 1 and 4%, but were dramatically decreasing when fed 15 and 25%. ALAT and ASAT were normal for animals fed 1 through 5%. Hepatic RE-cell proliferation, acidophilic degeneration and necrosis, hyalin bodies, and centrolobular steatosis were all dose-related in frequency and degree. Acidophilic degeneration occurred from 4% and above and hyalin bodies from 3% and above. Nephrocalcinosis was not dose-related. Tubular fatty changes tended to increase with dose.

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## INTRACELLULAR REDOX STATE AND GLUCONEOGENESIS OF PERFUSED RAT LIVER WITH HYDRAZINE-INDUCED MEGAMITOCHONDRIA

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Megamitochondria are well known to be induced by various compounds. However, data on the phosphorylating capacities of megamitochondria induced by various conditions, are still controversial.

The role of the cellular redox state in gluconeogenesis was studied in hemoglobin-free perfused male rat liver with megamitochondria induced by hydrazine:

The decreases in glucose production from lactate or sorbitol were noted. On the other hand, the glucose production from pyruvate, dehydrogenated substrate, was not decreased. Therefore, the maximum rate of glucose production from lactate/pyruvate (P/L) mixture in liver with megamitochondria was undetectable, while the maximum rate of glucose production from L/P mixture in non-treated liver was obtained with a L/P ratio of 10/1, which was comparable to the ratio in vitro using isolated hepatocytes.

The decreases in gluconeogenesis is ascribed to the decrease of NADH oxidation of megamitochondria.