

Title Nuclear metabolism of dimethylnitrosamine and its alteration during riboflavin deficiency.

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Abstract

The studies demonstrated the presence of DMN-metabolizing enzyme system in rat liver nuclei. This nuclear enzyme had the activity much lower than those of the microsomal fraction. Double-reciprocal plot of the enzyme kinetics suggested that it may be isozymes of low (1.11) and high (12.50) K_m s; the activities of both were decreased by PB pretreatment. However, only the low- K_m form (DMN-demethylase I) was inhibited by 3MC pretreatment.

Riboflavin deficiency enhanced the intro nuclear metabolism of DMN and this effect could be reversed by in vivo supplementation of riboflavin (0.5 mg/rat/day for 3 consecutive days). PB pretreatment exerted more inhibitory effect on the nuclear DMN-demethylase I activity of the riboflavin deficient rats while it increased the activity of the high K_m enzyme (DMN-demethylase II), 3MC pretreatment inhibited both DMN-demethylase I and II activities in riboflavin deficient rats.

Riboflavin deficiency also increased the amount of DMN metabolite bound to total macromolecular and DNA, but did not significantly alter the conversion of DMN to CO_2 . Acute toxicity of DMN as measured by the LD_{50} doses and SGPT and SGOT levels was decreased in riboflavin deficient rats indicating that these animals become less susceptible to the cytotoxic effect of DMN.