

# Abstract

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## Riboflavin Deficiency in Rats Decreases de novo Formate Production but Does Not Affect Plasma Formate Concentration.

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**BACKGROUND:** The one-carbon metabolism pathway is highly dependent on a number of B vitamins in order to provide one-carbon units for purine and thymidylate biosynthesis as well as homocysteine remethylation. Previous studies have examined folate and vitamin B-12 deficiency and their effects on formate metabolism; as of yet, to our knowledge, no studies on the effects of riboflavin deficiency on formate metabolism have been published.

**OBJECTIVE:** Our objective was to determine the effects of riboflavin deficiency on formate metabolism.

**METHODS:** Weanling male rats were randomly assigned either to control, riboflavin-replete (RR) or to experimental, riboflavin-deficient (RD) versions of the AIN-93G diet for 13 d, at which time a constant infusion of [<sup>13</sup>C]-formate was carried out to ascertain the effects of deficiency on formate production. Gas chromatography-mass spectrometry was used to measure plasma formate concentration and [<sup>13</sup>C]-formate enrichment. HPLC, LC-mass spectrometry (MS)/MS, and enzymatic assays were used for the measurement of one-carbon precursors and other metabolites.

**RESULTS:** RD rats had significantly lower rates of formate production (15%) as well as significantly reduced hepatic methylenetetrahydrofolate reductase activity (69%) and protein concentration (54%) compared with RR rats. There was no difference in plasma formate concentrations between the groups. Plasma serine, a potential one-carbon precursor, was significantly higher in RD rats (467 ± 73 μM) than in RR rats (368 ± 52 μM).

**CONCLUSIONS:** Although deficiencies in folate and vitamin B-12 lead to major changes in plasma formate concentrations, riboflavin deficiency results in no significant difference; this disagrees with the prediction of a published mathematical model. Our observation of a lower rate of formate production is consistent with a role for flavoproteins in this process.

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