3. Title: "The conversion of 2-hydroxy-4-methyl thiobutyric acid to methionine by rat tissue in vitro"

Principal Investigator: Bernhardt W. Langer, Jr., Ph.D.

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Objective:

To study the conversion of an unnaturally occurring compound (2-hydroxy-4-methylthiobutyric acid (MHA) into methionine, thereby providing general insight into the enzymatic alteration of other unnatural compounds such as drugs.

Method:

Using rat liver preparations and commercially available enzymes, the production of methionine and various intermediates in the conversion of MHA into methionine was studied. Methionine was measured microbiologically as described by Langer and Kratzer[1] while other intermediates were measured spectrophotometrically and chromatographically.

Progress:

Since the initiation of this projcet it has been found that rabbit muscle lactic dehydrogenase (LDH) will catalyze the reduction of DPN using MHA as a substrate. The product of this reaction has been postulated to be alpha-keto methionine. The Km for this reaction has been estimated to be around 50-100 umoles/3.2 ml.

As LDH catalyzes the conversion of alpha-keto forms to alpha-hydroxy forms more readily then the reverse, further work has awaited the synthesis of alpha-oxo-4-methylthiobutyric acid. This synthesis is currently being conducted using the method of Cahill and Rudolph[2]. The reduction of this alpha-keto acid will be followed spectrophotometrically using rabbit muscle LDH and preparations from rat liver.

Summary:

Rabbit muscle lactic dehydrogenase catalyzes the reduction of DPM with MHA as a substrate. The estimated Km for the substrate is 1.5 to 3.1 mmolar.

(1) B.W. Langer, Jr. and F.H. Kratzer, Poultry Science 43:127 (1964)
(2) W.M, Cahill and G.G. Rudolph, J. Biol. Chem. 145:201 (1942)