Carnitine Biosynthesis

β-HYDROXYLATION OF TRIMETHYLLYSINE BY AN α-KETOGLUTARATE-DEPENDENT MITOCHONDRIAL DIOXYGENASE*

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Rat liver mitochondria were found to hydroxylate ε-N-trimethyl-L-lysine to produce β-hydroxy-ε-N-trimethyl-L-lysine, an intermediate in carnitine biosynthesis. The hydroxylating system requires α-ketoglutarate, Fe²⁺, and ascorbate, but does not require NADPH nor NADH. No activity was found in the microsomal or soluble fractions of liver extracts. The hydroxylated α-amino acid was isolated and characterized by column chromatography using Dowex 50-H⁺ and Chelex 100–Cu²⁺ resins and by high voltage paper electrophoresis. The enzymatically produced β-hydroxy-ε-N-trimethyl-L-lysine was shown to be peroxidase-sensitive and one periodation product was characterized as γ-butyrobetaine aldehyde. The hydroxylated product was acted upon by crystalline serine transhydroxymethylase (EC 2.1.2.1) to yield γ-butyrobetaine aldehyde and glycine. Conversion of about 40% of the ε-N-trimethyl-L-lysine to β-hydroxy-ε-N-trimethyl-L-lysine was accomplished by this system with little or no further metabolism.

It is well documented that L-carnitine plays an important role in the translocation of both short and long chain fatty acids across the mitochondrial membrane to facilitate fatty acid synthesis and degradation (1, 2). Although carnitine is not a vitamin for most animals, the pathway by which it is synthesized has not been fully elucidated. It has been shown that the carbon chain and quaternary nitrogen atom are derived from C₂ and the ε-nitrogen of lysine and that the methyl groups are derived from methionine via the S-adenosylmethionine system (3, 4). Thus ε-N-trimethyl-L-lysine is an established precursor of γ-butyrobetaine (4-N-trimethylaminoethanesulfonic acid), α-ketoglutarate, sodium ascorbate, α-N-acetyl-L-lysine, bovine serum albumin, NADPH, NADH, catalase (EC 1.11.1.6), and digitonin were purchased from Sigma Chemical Co. 4-Aminobutyraldehyde diethyl acetal and iodomethane were purchased from Aldrich Chemical Co. The Dowex 50-X8 (200 to 400 mesh) and Chelex 100 (200 to 400 mesh) were purchased from Bio-Rad Laboratories and the [methyl-14C]iodide (56 &i/mol) was obtained from Amersham-Searle Corp. The Dowex 50-X8 (200 to 400 mesh) and Chelex 100 (200 to 400 mesh) were purchased from Bio-Rad Laboratories and the [methyl-14C]iodide (56 &i/mol) was obtained from Amersham-Searle Corp. The Dowex 50-X8 (200 to 400 mesh) and Chelex 100 (200 to 400 mesh) were purchased from Bio-Rad Laboratories and the [methyl-14C]iodide (56 &i/mol) was obtained from Amersham-Searle Corp.

Mitochondrial Isolation and Incubation - Rats, fed ad libitum Purina rat chow, were decapitated and their livers were quickly removed and placed on ice. The liver was weighed, cut into small pieces, and forced through a Harvard Apparatus tissue press. There are three volumes of the isolation buffer, containing 0.25 M sucrose, 0.05% bovine serum albumin, 2.0 mM Hepes, pH 6.8, were added to the liver mince and homogenized with a motor-driven loose fitting Potter-Elvehjem homogenizer making two passes. The remainder of the procedure was basically as described by Schnaitman and Greenwald (12); the mitochondria were pelleted at 9000 × g. The microsomes were obtained by further centrifugation at 100,000 × g. The mitochondria were washed and resuspended in isolation medium so that 3 ml contained the mitochondria from 1 g of liver; this suspension was used directly in the mitochondrial incubations.

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1 The abbreviation used is: Hepes, 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid.
supernatant and washing were fractionated on a Dowex 50-H+ column. Two 5.0-ml portions of 3.0 M HCl were packed with Dowex 50-H+ resin and washed with H₂O. The ethanol extracts were then washed well with H₂O. The sample was applied and the column was developed as described in the text.

Separation of 14C Products - Glass columns (1.4 x 50.0 cm) were packed with Dowex 50-H+ resin and washed with H₂O. The ethanol treated sample from the incubation mixture was placed on the column and developed with: (a) two 5.0-ml portions of 3 M HCl, (b) a linear gradient using 200 ml each of 1.5 M and 5.0 M HCl. The trimethyllysine metabolites were well separated as shown in Fig. 2.

The Chelex 100 resin formed a complex with Cu²⁺ and the ammonia ligand was added as described by Goldstein (13). Short (2.5 cm) columns (diameter, 1.1 cm) were packed with the resin which was then washed well with H₂O. The sample was applied and the column was developed with: (a) two 5.0-ml portions of H₂O, (b) two 5.0-ml portions of 3 M NH₄OH, and (c) two 5.0-ml portions of 0.5 M NaCl. The water wash contained compounds such as γ-butyrobetaine and carnitine which were not α-amino acids and which had insufficient net positive charge to allow them to adhere ionically to uncomplexed iminoacetic acid groups of the resin. The ammonia displaced α-amino acids such as trimethyllysine and β-hydroxy-ε-N-trimethyl-L-lysine (hydroxytrimethyllysine) as ligands to the copper complex. The salt wash eluted metabolites such as γ-butyrobetaine aldehyde that were ionically attached to the column and not displaced by ammonia. Samples of each cluant were counted by liquid scintillation spectrometry using scintillation fluid containing 40% absolute ethanol and 60% toluene with 4.0 g of 2,5-diphenyloxazole (PPO) and 0.2 g of 1,4-bis[2-(5-phenyloxazolyl)]benzene (POPOP)/liter.

For paper chromatography the samples were spotted at one end of a sheet of Whatman No. 3MM paper and electrophoresed toward the cathode using a Savant high voltage electrophoresis apparatus. The buffer used was 0.05 M acetic acid adjusted to pH 5.1 with pyridine and the sheets were electrophoresed for 90 min at 2000 V. The sheets were cut into strips and the radioactivity was located using a Packard radiochromatogram scanner which gave profiles such as that shown in Fig. 3.

Initial attempts to detect the enzyme which hydroxylates trimethyllysine revealed no activity in the microsomal or soluble fractions but considerable activity was located in the mitochondrial fraction of rat liver and kidney. Further treatment of the mitochondria with 0.01% Triton X-100, a surfactant, for 1.0 h to partially destroy the integrity of the mito-

RESULTS

Initial attempts to detect the enzyme which hydroxylates trimethyllysine revealed no activity in the microsomal or...
Table I: Products from incubation of trimethyllysine with mitochondria

The standard consists of a mixture identical with that described under "Experimental Procedures." The supernatant fraction has 3.0 ml of the supernatant from the first 8300 rpm centrifugation (soluble proteins and microsomes) in place of the 3.0 ml of mitochondrial suspension. In the three mixtures where one component has been omitted 2 mM Hepes, pH 6.8, has been added to keep the volume constant. The citrate was used as the same concentration as the α-ketoglutarate replaced. The Hepes samples contain mitochondria resuspended in 2 mM Hepes, pH 6.8 (not containing bovine serum albumin or sucrose). The NADH and NADPH solutions used to replace α-ketoglutarate were 0.01 M and the dithiothreitol solution used to replace ascorbate was 0.04 M.

<table>
<thead>
<tr>
<th>Variation in incubation mixture</th>
<th>% of metabolite recovered as</th>
<th>Trimethyllysine</th>
<th>Hydroxytrimethyllysine</th>
<th>γ-Butyrobetaine and carnitine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td></td>
<td>60.9</td>
<td>34.2</td>
<td>4.9</td>
</tr>
<tr>
<td>Supernatant fraction</td>
<td></td>
<td>99.3</td>
<td>0.71</td>
<td>0.77</td>
</tr>
<tr>
<td>Omit α-ketoglutarate</td>
<td></td>
<td>100</td>
<td>0.71</td>
<td></td>
</tr>
<tr>
<td>Omit FeSO₄</td>
<td></td>
<td>99.2</td>
<td>0.83</td>
<td></td>
</tr>
<tr>
<td>Omit sodium ascorbate</td>
<td></td>
<td>100</td>
<td>0.79</td>
<td></td>
</tr>
<tr>
<td>Citrate replaced α-ketoglutarate</td>
<td></td>
<td>99.2</td>
<td>0.79</td>
<td></td>
</tr>
<tr>
<td>Hepes (lysed mitochondria)</td>
<td></td>
<td>55.9</td>
<td>39.2</td>
<td>4.85</td>
</tr>
<tr>
<td>Hepes, NADH replaced α-ketoglutarate</td>
<td></td>
<td>100</td>
<td>0.71</td>
<td></td>
</tr>
<tr>
<td>Hepes, NADPH replaced α-ketoglutarate</td>
<td></td>
<td>100</td>
<td>0.79</td>
<td></td>
</tr>
<tr>
<td>Dithiothreitol replaced ascorbate</td>
<td></td>
<td>99.8</td>
<td>0.2</td>
<td></td>
</tr>
</tbody>
</table>

* These are per cents of total radioactivity recovered; the total corresponds to 93 to 99% of the dose.

† Both carnitine and γ-butyrobetaine elute from the column in the 1.5 N HCl wash and were not separated in these experiments.

that the hydroxylase is located in the outer membrane. Acetone powder preparations of the mitochondria were active when suspended in 2.0 mM Hepes buffer, pH 6.8.

A typical elution profile of the Dowex 50 fractionation of an incubation mixture is shown in Fig. 4. A minor peak was observed at the elution volume corresponding to standard γ-butyrobetaine (A) (compare Fig. 2). The major metabolite (B) eluted from the column during the 1.5 to 5.0 N HCl gradient at a volume between that of standard trimethyllysine (C) and α-N-acetyl-ε-N-trimethyllysine (485 ml). It has been reported (14) that α-hydroxy-ε-N trimethyl-L-lysine elutes from a similar column at a volume just after α-N-acetyltrimethyllysine, a major metabolite from whole animal experiments. An hydroxylated product is also consistent with the postulated scheme (Fig. 1) and with the hydroxylation cofactors required in the incubation mixture. To characterize this component the appropriate tubes were pooled and the HCl was removed by lyophilization. The elution of this metabolite from a Chelex 100-Cu²⁺ column by 3 N NH₄OH (Table II) indicated that it was an α-amino acid. During paper electrophoresis the metabolite co-migrated with trimethyllysine which might be expected because of the similarity in structure of trimethyllysine and hydroxytrimethyllysine. Attempts to separate the two compounds by high voltage paper electrophoresis at both acidic and basic pH values have not been successful.

Periodate treatment of the mitochondrial product resulted in one or two new products, depending on the concentration of periodate and the reaction time. Following the procedure described above, a product was obtained that remained on the Chelex 100-Cu²⁺ column during both the H₂O and NH₄OH washes, but was eluted from the column with 0.5 N NaCl (Table II). This suggested a peridate product that was not an α-amino acid, as was the metabolite prior to periodation, but was a product with sufficient net positive charge to adhere to the column. The expected periodate product of hydroxytrimethyllysine, γ-butyrobetaine aldehyde, would be expected to exhibit this behavior on the Chelex column. Also, it is important to note (Table II) that it was not simple oxidation of the α-amino acid during periodate treatment that resulted in this change since the similar α-amino acid, trimethyllysine, was unaffected by periodation.

This periodation product was characterized by paper electro-
y-butyrobetaine and ϵ-N-trimethyl-L-lysine were placed on separate columns and developed as above. The periodation product was also fractionated on a Dowex 50-H+ column, but it appeared at the same peak effluent volume as did y-butyrobetaine.

To identify further the periodation product, ϵ-N-[methyl-14C]trimethylaminobutyraldehyde (y-butyrobetaine aldehyde) was synthesized and used as a standard. It would not be eluted with 0.5 N NaCl. From a Dowex 50-H+ column, it appeared in the same peak effluent volume as y-butyrobetaine and it migrated about 36 cm during electrophoresis at pH 5.1 but are sufficiently dissimilar that they might be expected to separate under these conditions.

The periodation product was also fractionated on a Dowex 50-H+ column, but it appeared at the same peak effluent volume in the 1.5 N HCl eluate as did y-butyrobetaine. Pooling the fractions in this peak and subjecting them to paper electrophoresis gives a separation of the aldehyde (36 cm) and y-butyrobetaine (19 cm). When higher concentrations of periodate (0.5 M) were used the product obtained was different. It behaved like y-butyrobetaine on the Chelex 100-Cl- column, paper electrophoresis and Dowex 50-H+ column. y-Butyrobetaine is the product Hoppel et al. (14) reported finding upon periodation of hydroxytrimethyllysine.

To identify further the periodation product, ϵ-N-[methyl-14C]trimethylaminobutyraldehyde (y-butyrobetaine aldehyde) was synthesized and used as a standard. It would not elute from the Chelex 100-Cu2+ column with either H2O or 3 M NH4OH but was eluted with 0.5 M NaCl. From a Dowex 50-H+ column, it appeared in the same peak effluent volume as y-butyrobetaine and it migrated about 36 cm during electrophoresis at pH 5.1. Thus, it behaved in an identical manner to the periodated mitochondrial product in all three systems.

The mitochondrial hydroxylation product, tentatively identified as hydroxytrimethyllysine, is a substrate for crystalline serine transhydroxymethylase. The product of this reaction has been identified as y-butyrobetaine aldehyde using the Chelex 100-Cu2+ and Dowex 50 columns, and high voltage paper electrophoresis. Thus, three distinct methods have been used to produce y-butyrobetaine aldehyde. This aldehyde is oxidized by KMnO4 to yield a product identified by high voltage paper electrophoresis as y-butyrobetaine (Fig. 5C).

To substantiate further the scheme shown in Fig. 1, ϵ-N-trimethyl-L-[carboxy-14C]lysine (6) was used to produce [carboxy-14C]hydroxytrimethyllysine. This hydroxytrimethyllysine was incubated with crystalline serine transhydroxymethylase for 90 min and then nonradioactive glycine was added to the reaction mixture. Glycine was isolated and recrystallized from the mixture, using aqueous ethanol, to constant specific activity, thus confirming that glycine was the two carbon fragment released by serine transhydroxymethylase. To demonstrate the physiological significance of hydroxytrimethyllysine as a carnitine precursor it was incubated with a crude rat liver homogenate and the results are shown in Table III. Hydroxytrimethyllysine was readily converted to y-butyrobetaine and a minimal amount of carnitine. In contrast this crude system did not act on trimethyllysine although all of the hydroxylating cofactors had been added.

**DISCUSSION**

ϵ-N-Trimethyl-L-lysine is an established precursor of L-carnitine, but it has been difficult to obtain an isolated organ or otherwise simplified system that would take up and metabolize trimethyllysine as does the whole animal. It appears that

### Table II

**Separation of trimethyllysine metabolites on a Chelex 100-Cu2+ column**

Approximately 35,000 dpm each of carnitine and mitochondrial product (δ-hydroxy-ε-N-trimethyl-L-lysine) and 53,000 dpm each of y-butyrobetaine and ϵ-N-trimethyl-L-lysine were placed on separate Chelex 100-Cu2+ columns and developed with 10 ml each of (a) H2O, (b) 3 N NH4OH, (c) 0.5 M NaCl. Duplicates of the four samples were periodated using 10 μl of sample, 10 μl of 0.01 M NaIO4, and 4 μl of 5.0 mM NaOAc, allowing 5 min for the reaction to occur before placing them on columns and developing as above.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Total dpm in</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H2O</td>
</tr>
<tr>
<td>Carnitine</td>
<td>34,800</td>
</tr>
<tr>
<td>γ-Butyrobetaine</td>
<td>52,250</td>
</tr>
<tr>
<td>ε-N-Trimethyl-L-lysine</td>
<td>190</td>
</tr>
<tr>
<td>Mitochondrial product</td>
<td>580</td>
</tr>
<tr>
<td>Carnitine + IO4−</td>
<td>32,700</td>
</tr>
<tr>
<td>γ-Butyrobetaine + IO4−</td>
<td>52,870</td>
</tr>
<tr>
<td>ε-N-Trimethyl-L-lysine + IO4−</td>
<td>290</td>
</tr>
<tr>
<td>Mitochondrial product + IO4−</td>
<td>1,270</td>
</tr>
</tbody>
</table>

**Fig. 5.** Electrophoresis patterns of the [methyl-14C]hydroxytrimethyllysine following treatment with periodate (A) and following oxidation of the periodate product with permanganate (C). B depicts the migration of authentic γ-butyrobetaine Peak A, unresolved hydroxytrimethyllysine Peak B, and periodated treated hydroxytrimethyllysine Peak C.

**Table III**

**Metabolism of carnitine intermediates by a rat liver homogenate**

<table>
<thead>
<tr>
<th>Substrate</th>
<th>% recovered as</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carnitine</td>
</tr>
<tr>
<td>ε-N-Trimethyllysine</td>
<td>100</td>
</tr>
<tr>
<td>14C-Hydroxy-ε-N-trimethyllysine</td>
<td>0</td>
</tr>
<tr>
<td>Carnitine</td>
<td>58.7</td>
</tr>
<tr>
<td>β-Hydroxy-ε-N-trimethyllysine</td>
<td>0</td>
</tr>
</tbody>
</table>

### Table III

**Metabolism of carnitine intermediates by a rat liver homogenate**

One gram of rat liver was homogenized with 2.0 ml of 2 mM Hepes buffer, pH 6.8, and 86 μl of 0.1 M sodium ascorbate, 103 μl of 0.1 M α-ketoglutarate, and 103 μl of 5.0 mM ferrous sulfate were added. Either 0.25 μmol of ε-N-trimethyllysine or 0.25 μmol of β-hydroxy-ε-N-trimethyllysine (both had specific activity of 37 mCi/μmol) was added, the sample was incubated at 37° for 3 h, and then the reaction was stopped with ethanol and products were resolved on a Dowex 50-H+ column as previously described.
impermeability of the cell to trimethyllysine is the reason for this apparent metabolic inertness. The preliminary experiments for this report showed that lengthy exposure of either liver or kidney slices to trimethyllysine resulted in very little uptake of the substrate. This is consistent with the reports of others (9, 10). Perfusion of liver and kidney for 2-h periods during which the tissue was continually exposed to the substrate by recirculation through the vascular system also resulted in little or no conversion. On the other hand, LaBadie et al. (15) have done liver perfusion experiments using 14C-methylated acetaldehyde, which is readily taken up by the liver and hydrolyzed to yield intracellular trimethyllysine. They found 30% of the added isotope in carnitine after 90 min of perfusion. In the experiments reported here, destruction of liver or kidney cells and subsequent isolation of mitochondria also resulted in a system that effected a significant conversion of trimethyllysine to β-hydroxymethyl-lysine, when appropriate hydroxylating cofactors were added.

This hydroxylation does not make use of the most common cofactors of hydroxylating systems, NADH or NADPH, nor is it associated with the micosomal fraction as is more common for mixed function oxidases. Similar α-ketoglutarate-dependent systems have been reported for the hydroxylation in animals of γ-butyrobetaine yielding carnitine (16), of lysyl and prolyl residues in collagen precursors (17, 18), and in Neurospora crassa of pyrimidine deoxyribonucleoside (19), and of three sequential reactions on thymine yielding uracil-5-carboxylic acid (20). This appears to be the first α-ketoglutarate-dependent dioxygenase found in the mitochondria. Studies of Lindstedt and Lindstedt (16) on the γ-butyrobetaine hydroxylase demonstrated increased activity when catalase was added to the system; this is most likely due to destruction of H₂O₂ produced by Fe²⁺-catalyzed autooxidation of ascorbate (21). Although no stimulation from adding catalase was observed in this study, the decrease in activity noted when the concentration of ascorbate was increased in the liver slices used by Lindstedt and Lindstedt (16), could be the result of enzyme inactivation by H₂O₂.

The possibility that α-ketoglutarate functions merely because it is capable of entering mitochondria where it is subsequently converted to succinate, producing NADH for hydroxylation, was considered. As has been shown in Table 1, another tricarboxylic acid cycle intermediate, citrate, could not replace α-ketoglutarate. Although citrate could be converted to α-ketoglutarate via the tricarboxylic acid cycle, the α-ketoglutarate so produced would not accumulate to high enough concentrations to promote hydroxylation. However, the NADH so produced would be at approximately the same concentration as if arising from α-ketoglutarate oxidation. Mitochondrial fragments which functioned with added α-ketoglutarate were inactive when NADH or NADPH replaced α-ketoglutarate. α-Ketoglutarate therefore seems to be an essential component of this reaction, functioning as described in the previously mentioned α-ketoglutarate-dependent hydroxylases. Also consistent with this type of hydroxylation are the requirements of Fe²⁺ and ascorbate. In characterizing the α-ketoglutarate dioxygenases listed above, the α-ketoglutarate and Fe²⁺ requirements have been found to be highly specific (22–20). Reducing agents other than ascorbate can function, but ascorbate is more effective in each of the reactions.

The product of the mitochondrial incubations has been identified as β-hydroxy-γ-N-trimethyllysine using Dowex 50-H⁺ columns, Chelex 100-Cu²⁺ columns and periodation followed by paper electrophoresis and Chelex 100-Cu²⁺ columns. Hoppel et al. (14) isolated a small amount of hydroxytrimethyllysine from large volumes of urine from rats injected with large doses of trimethyllysine. They reported its elution from a Dowex 50-H⁺ column between trimethyllysine and α-N-acetylimethyllysine; this is the same relative position as the product described here, although a somewhat different elution procedure was used. It has been shown that the product of this hydroxylation is an α-amino acid by its retention on a Chelex 100-Cu²⁺ column and subsequent elution with 3 N NH₄OH. The periodate sensitivity of this compound has been demonstrated using mild enough conditions that α-amino acids would not be affected. These data indicate that the hydroxylating system used has produced a metabolite which has a hydroxyl group in a vicinal position to the α-amino group. Further characterization by paper electrophoresis and Chelex 100-Cu²⁺ chromatography of the periodation product has led to the conclusion that it is γ-butyrobetaine aldehyde and hence the product of mitochondrial enzyme is hydroxytrimethyllysine. Although periodation of hydroxytrimethyllysine has been reported to yield γ-butyrobetaine (14), milder conditions have been shown here to give the aldehyde. The identity of the periodation product has been verified by synthesis of the aldehyde then comparing its behavior during Chelex 100-Cu²⁺ and Dowex 50-H⁺ column chromatography and on high voltage paper electrophoresis. The physiological significance has been demonstrated by showing production of the same aldehyde by reaction of hydroxytrimethyllysine with crystalline serine transhydroxymethylase.

This report is the first to present an isolated system from liver that efficiently converts trimethyllysine to another precursor of carnitine. Cox and Hoppel (10) reported a kidney slice system that yielded 18% γ-butyrobetaine from trimethyllysine, but this tissue did not catalyze the next reaction to produce carnitine (9, 10, 27). Hydroxylation of trimethyllysine by other tissues, including liver, which is also capable of hydroxylating γ-butyrobetaine, has been tried, but only 1 to 2% or less of the trimethyllysine has been metabolized (9, 10). The conversion reported here is near 40% using hydroxylating cofactors. The hydroxytrimethyllysine thus produced has also been shown to be an effective precursor for carnitine as demonstrated by the 60% conversion to carnitine and its immediate precursors in a 3-h experiment with crude rat liver homogenates. Indicative of the problem previously encountered, the same crude homogenate system was totally ineffective in metabolizing trimethyllysine to any other carnitine precursor, possibly reflecting the sensitivity of the enzyme to the proteases. One report (28) suggests another scheme by which trimethyllysine might be converted to carnitine, but this work was done with Neurospora crassa and the data reported here are not consistent with that scheme.

REFERENCES
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