
LETTERS TO THE EDITORS

α -AMINOADIPIC ACID: A PRODUCT OF LYSINE METABOLISM*†

Sirs:

As part of a study of protein and peptide metabolism lysine was synthesized with C^{14} in the ϵ position and resolved into the L and D isomers. 10 mg. of labeled lysine dihydrochloride (either L- or D-) and 0.66 gm. (wet weight) of guinea pig liver homogenate were added to a reaction mixture containing 1.3 per cent of an amino acid mixture corresponding to the composition of casein except for lysine and 0.01 M α -ketoglutarate, all in a final volume of 4 ml. of isotonic saline solution.¹ The reaction was carried out under oxygen for 6 hours at 38°.

After precipitation of the proteins by boiling at pH 5.0, a fraction of the non-protein filtrate was chromatographed on filter paper.² Ninhydrin gave a lysine spot which was radioactive and another radioactive spot in the glutamic acid region. This indicated the presence of a dicarboxylic α -amino acid different from glutamic acid, since to obtain glutamic acid from the labeled lysine would entail removing the radioactive ϵ -carbon.

The chromatographic behavior of this radioactive substance on filter paper and on Lloyd's reagent suggested, in view of the source of the C^{14} , that the unknown substance might be α -aminoadipic acid. Accordingly the latter was synthesized; it gave the same filter paper chromatogram as the unknown.

Radioactive α -aminoadipic acid (probably mixed with glutamic acid) was isolated from the reaction mixture as a barium salt by the following procedure. After hydrolysis of the non-protein filtrate with hydrochloric acid and chromatography on Lloyd's reagent,³ whereby the hexone bases were removed, the non-basic amino acid fraction was precipitated with barium from 75 per cent ethanol. The barium was removed from the precipitate, and the dicarboxylic acids again precipitated with barium. 99 per cent of the radioactivity originally present in the fraction was found in

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† The C^{14} used in this investigation was supplied by the Monsanto Chemical Company, Clinton Laboratories, and obtained on allocation from the United States Atomic Energy Commission.

¹ Borsook, H., and Dubnoff, J. W., *J. Biol. Chem.*, **171**, 363 (1947).

² Consden, R., Gordon, A. H., and Martin, A. J. P., *Biochem. J.*, **38**, 224 (1944).

³ Bergdoll, M. S., and Doty, D. M., *Ind. and Eng. Chem.*, **18**, 600 (1946).

this barium precipitate. The barium was again removed, and a fraction obtained by crystallization from 20 per cent hydrochloric acid was washed, dried, and then chromatographed on filter paper. One strong spot was obtained with ninhydrin in the same position as that of the original unknown; it contained all the estimated amount of radioactivity. Two other very faint spots were obtained, one of which corresponded to aspartic acid, the other to alanine or threonine; neither had radioactivity. There was no lysine spot, nor was there any radioactivity in the region of the lysine spot.

The above evidence is conclusive, short of isolation of the compound, that lysine is deaminated in the ϵ position to α -aminoadipic acid.

The following evidence showed that the process is an enzymatic one and added to the proof that the radioactivity did not come from contamination by the labeled lysine originally added. The dicarboxylic acid fraction contained no radioactivity when the homogenate was first boiled; much more radioactivity was found when the reaction was carried out at pH 7.5 than at 8.2 and with the L than with the D form of lysine. The activity found with the latter may be due entirely to the presence of a small amount (10 per cent or less) of the L form remaining after resolution.

Under our best conditions so far 1 γ of lysine is converted to α -aminoadipic acid per 10 mg. (dry weight) of guinea pig liver homogenate per hour.

In an accompanying communication evidence is presented that lysine is converted to α -aminoadipic acid in rat kidney slices. Dr. H. K. Mitchell kindly tested the ability of synthetic DL- α -aminoadipic acid to replace lysine in a *Neurospora lysineless* mutant. It was able to do so.⁴

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⁴ Mitchell, H. K., and Houlahan, M. B., unpublished observation.