11593

Metabolism of α,β- and β,γ-Deuterocaproic Acids.*

MARGARET G. MOREHOUSE AND H. J. DEUEL, JR.

From the Department of Biochemistry, University of Southern California Medical School, Los Angeles.

In earlier studies it has been demonstrated that deuterium may be retained on the betahydroxybutyrate molecule excreted after feeding deuterobutyric acid to rats.[1] When the α,β-dideutero acid was fed, only 4.2 atoms% were retained, while after feeding the β,γ-dideuterobutyric acid, an average of 22.5% of the excreted betahydroxybutyrate contained deuterium.

In order to determine which part of the caproic acid molecule is convertible to acetone bodies, a study of the deuterium content of betahydroxybutyric acid excreted in the urine after the feeding of the α,β- and β,γ-dideuterocaproate has been made. The deutero acids were prepared by saturation of the corresponding unsaturated acids.

The α,β unsaturated acid was formed by condensation of butyraldehyde and malonic acid under the influence of pyridine as a base while the formation of the β,γ hexenoic acid was a condensation of the same substances with triethanolamine as a base. They were identified by saponification numbers, boiling points, indices of refraction, and the rate of iodine uptake of the acids and their corresponding ethyl esters.

The acids were fed by stomach tube in the form of their sodium salts to female rats previously fasted 72 hours. The amounts administered were equivalent to 150 mg per 100 sq cm (calculated as acetone) per day in 2 divided doses. The urines of 8 animals were pooled, the betahydroxybutyric acid separated by acidification, extraction in butyl alcohol, and the subsequent extraction from this material as the sodium salt by means of sodium carbonate. The silver salt was then prepared. This was analyzed for betahydroxybutyric acid and its deuterium content. The results are shown in Table I.

A production of acetone bodies was found to occur after the feeding of the 2 dideuterocaproic acids. The amounts recovered on the fourth day of the fast as betahydroxybutyric acid varied from

* This work was made possible by a research grant from The Best Foods, Inc.

1 Morehouse, M. G., *J. Biol. Chem.*, 1939, **129**, 769.

TABLE I.
Excretion of Deutero-β-hydroxybutyrate After Feeding Deuterocaproic Acids.

Exp. No.*	Amt of deutero-caproate fed as acetone	Acetone bodies excreted as acetone in mg			% of total as β-hydroxy-butyrate	β-hydroxy-butyrate excreted as such	Analysis of Ag β-hydroxybutyrate		% of caproate fed excreted as acetone
		β-hydroxy-butyrate	Diacetic	Total			% β-hydroxy-butyrate	Atoms % of deuterium	
				αβ-deuterocaproic acid.					
	mg					mg			
1-4	2928	1194	338	1532	77.9	2150	99.7	6.77	52.3
2-4	2844	1373	341	1714	80.1	2462	96.7	4.95	60.3
1-5	2928	1354	408	1762	76.9	2427	98.5	7.05	60.2
2-5	2844	1498	428	1926	77.8	2688	99.7	6.95	67.7
Avg					78.2		98.8	6.43	
				βγ-deuterocaproic acid.					
3-4	2877	1400	500	1900	73.7	2510	98.9	13.07	66.0
4-4	2855	1442	483	1925	74.9	2584	96.1	8.95	67.4
3-5	2877	1594	576	2170	73.4	2858	96.1	11.82	75.4
4-5	2855	1753	615	2368	74.0	3143	96.4	9.71	82.9
Avg					74.0		96.9	10.89	

*The second number represents the day of the fast.

†Calculated by the factor 9.51 for mg of mercury precipitate equivalent to 1 mg hydroxybutyrate (Blunden, H., Hallman, L., Morehouse, M. G., and Deuel, H. J., Jr., *J. Biol. Chem.*, 1940, **135**, 757).

52.2 to 66.7% of that fed. On the following day the recovery was higher varying from 60.1 to 82.7%. The animals fed the β,γ-dideutero acid excreted in all cases slightly higher proportions than did those which received the α,β compound.

The analyses of the silver salts of betahydroxybutyrate showed a sufficient purity that it would be impossible for the deuterium present to be in the form of a contaminant.

The analysis for deuterium indicates that in the case of the rats fed α,β-deuterocaproate an average of 6.43% of the betahydroxybutyric acid excreted contained deuterium (calculated on the basis of one atom to a molecule of acid). Those receiving the β,γ-caproate excreted a hydroxy acid which averaged 10.89% of the deutero-containing acid.

If the betahydroxybutyrate had originated from the α,β-deuterocaproate solely by beta oxidation, then no deuterium would be present because the β carbon atom containing the deuterium would be replaced by a carboxyl group. The retention of deuterium which did occur can best be explained on the basis of a delta oxidation. On the other hand the higher deuterium content occurring after feeding the β,γ-deuterocaproate would also seem to indicate that delta oxidation had played a part. Inasmuch as the deuterium is retained to a greater extent when on the γ carbon than on the α carbon atom in betahydroxybutyrate,[1] the higher retention here can be explained as partly traceable to delta oxidation with a consequent retention of the deuterium on the γ position. These experiments would seem to indicate the probability that delta oxidation plays an important role in the oxidation of caproic acid.

11594

Reaction of Dog's Colon to Subcutaneous Injections of Morphine.

R. D. TEMPLETON, E. A. GALAPEAUX, AND H. F. ADLER

From the Departments of Physiology, Loyola University School of Medicine, and the University of Chicago.

An increase in intestinal tone following the administration of morphine seems to be the most consistent result reported by various investigators. According to Plant and Miller[1] the most pronounced and lasting effect of morphine upon the colon of unanesthesized

[1] Plant, O. H., and Miller, G. H., *J. Pharm. and Exp. Therap.*, 1927, **32**, 437.