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Amino Acid Metabolism. Fate of dl-Methionine in the Phlorhizinized Dog.

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The manifest interest in the metabolism of methionine makes it desirable to record the fate of this amino acid in phlorhizin diabetes. The generalizations to be derived from the fate of other amino acids (Lusk[1]) leads one to suspect that methionine can act as a glucose former. The data to be presented indicate that dl-methionine can be metabolized to yield glucose in the phlorhizinized dog.

dl-Methionine was synthesized by the method of Windus and Marvel.*[2] Phlorhizin was administered by the Coolen[3] method. Urine was collected by catheterization. Nitrogen was determined by the usual Kjeldahl method, glucose by the Benedict method as described by Quick,[4] and sulfur and sulfates by the methods of Folin.[5] The amino acid was administered as the sodium salt, being injected subcutaneously in a volume of 140 cc. The data are summarized in Table I.

The sulfur is excreted slowly. Dakin[6] found similarly that the

TABLE I
Glucose Formation from Injected dl-Methionine in Phlorhizin Diabetes.

Period	hr.	Wt. Kilo	N Gm.	Glucose Gm.	D/N	Total S Gm.	Inorg. SO_4-S Gm.	Total SO_4-S Gm.	Extra Glucose Theory 3-Carbon Gm.	Extra Glucose Found Gm.
I*	24	7.7	6.00	20.56	3.42	.433	.285	.298		
II	24	7.5	7.09	23.00	3.25	.476	.292	.315		
III	12	7.1	4.36	15.16	3.48	.270	.158	.167		
IV†	12	7.3	4.68	17.56	3.75	.788	.306	.334	7.50	5.76
V	24	6.7	8.00	27.20	3.40	1.637	.718	.742		
VI	12	6.5	3.09	10.54	3.41	.429	.232	.250		

* Dog starved 3 days—receiving phlorhizin (1 gm.) for 1 day prior to period 1. Phlorhizin injected daily thereafter.

† 12.5 gm. dl-methionine injected subcutaneously (1.17 gm. N. 2.69 gm. S).

[1] Lusk, G., The Science of Nutrition, W. B. Saunders Co., 4th Ed., 1928.

* The amino acid was prepared in collaboration with Dr. R. W. Jackson, following supplementary directions received directly from Dr. Marvel.

[2] Windus, W., and Marvel, C. S., *J. Am. Chem. Soc.*, 1930, **52**, 2575.

[3] Coolen, F., *Arch. f. Pharm.*, 1895, **1**, 267.

[4] Quick, A. J., *Ind. Eng. Chem.*, 1925, **17**, 729.

[5] Hawk, P. B., and Bergeim, O., Practical Physiological Chemistry, P. Blakiston Son & Co., 9th Ed., 1926, 770.

[6] Dakin, H. D., *J. Biol. Chem.*, 1913, **14**, 321.

sulfur excretion after cysteine injection was relatively slow, recovering about 50% of the sulfur of the amino acid in the urine during 36 hours following the injection. In contrast to the results with cysteine the major portion of the methionine sulfur was excreted in the neutral sulfur fraction. The post-injection urines gave a positive reaction with Grote's[7] test for C-S-S-C compounds. The Sullivan test for cystine, as described by Brand, Harris and Biloon[8] gave questionable results. The presence of acetone bodies in the urine prevented the interpretation of the usual sodium cyanide-sodium nitroprusside test for S-S compounds.

7027 C

On the Mechanism of Sodium Depletion in Addison's Disease.

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The authors have made the following observations in relation to the development of acute adrenal insufficiency in Addison's disease: 1. There is a marked decrease in the concentration of sodium in the blood serum.[1] 2. The withdrawal of salt from the diet of a patient suffering from Addison's disease promptly induces symptoms of severe insufficiency.[2] 3. The administration of NaCl in large amounts brings about striking clinical improvement which may be correlated with a return of the Na content of the blood to a normal level.[1, 2] These findings have recently been confirmed by Harrop and his coworkers.[3, 4] 4. Sodium is lost from the body of adrenalectomized dogs as a result of augmented renal excretion of this element.[5] This observation has also been substantiated by Harrop.[6]

[7] Grote, I. W., *J. Biol. Chem.*, 1931, **93**, 25.

[8] Brand, E., Harris, M. M., and Biloon, S., *J. Biol. Chem.*, 1930, **86**, 315.

[1] Loeb, R. F., *Science*, 1932, **76**, 420.

[2] Loeb, R. F., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 808.

[3] Harrop, G. A., Weinstein, A., Soffer, L. J., Trescher, J. H., *J. Am. Med. Assn.*, 1933, **100**, 1850.

[4] Harrop, G. A., *J. Am. Med. Assn.*, 1933, **101**, 388.

[5] Loeb, R. F., Atchley, D. W., Benedict, E. M., Leland, J., *J. Exp. Med.*, 1933, **57**, 775.

[6] Harrop, G. A., Soffer, L. J., Ellsworth, R., and Trescher, J. H., *J. Exp. Med.*, 1933, **58**, 17.