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Pantothenic and Hydroxypantothenic Acids in Animal Nutrition.

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It is now known that the rat requires at least 4 specific factors of the vitamin B complex: thiamin, riboflavin, vitamin B₆, and pantothenic acid. Only recently has the structure of pantothenic acid been determined^{1, 2} and its synthesis accomplished,^{3, 4} but the need for this factor in animal nutrition is already fairly well established.

The identification of the chick antidermatitis factor as pantothenic acid was established independently by Woolley, Waisman and Elvehjem^{5, 6} and Jukes.⁷ Shortly thereafter, studies were undertaken by several groups of investigators to determine whether or not pantothenic acid was an essential factor in the nutrition of the rat. Subbarow and Hitchings^{8, 9} concluded that pantothenic acid was probably one of the active factors in their liver filtrate preparations which were necessary for rat growth. El Sadr and his associates¹⁰ also reported great similarity between their liver filtrate factor and pantothenic acid. Hoffer and Reichstein¹¹ demonstrated a rat-growth response to beta-alanine which these investigators suspect to be the active principle of the whole pantothenic molecule. Oleson, Woolley, and Elvehjem¹² found that crude preparations of pantothenic acid produced a growth response in rats fed a filtrate factor deficient diet.

¹ Williams, R. J., and Major, R. T., *Science*, 1940, **91**, 246.

² Stiller, E. T., Keresztesy, J. C., and Finkelstein, J., *J. Am. Chem. Soc.*, 1940, **62**, 1779.

³ Williams, R. J., Mitchell, H. K., Weinstock, H. H., Jr., and Snell, E. E., *J. Am. Chem. Soc.*, 1940, **62**, 1784.

⁴ Stiller, E. T., Harris, S. A., Finkelstein, J., Keresztesy, J. C., and Folkers, K., *J. Am. Chem. Soc.*, 1940, **62**, 1785.

⁵ Woolley, D. W., Waisman, H. A., and Elvehjem, C. A., *J. Am. Chem. Soc.*, 1939, **61**, 977.

⁶ Woolley, D. W., Waisman, H. A., and Elvehjem, C. A., *J. Biol. Chem.*, 1939, **129**, 673.

⁷ Jukes, T. H., *J. Am. Chem. Soc.*, 1939, **61**, 975.

⁸ Subbarow, Y., and Hitchings, G. H., *J. Am. Chem. Soc.*, 1939, **61**, 1615.

⁹ Hitchings, G. H., and Subbarow, Y., *J. Nutrition*, 1939, **18**, 265.

¹⁰ El Sadr, M. M., Hind, H. G., Macrae, T. F., Work, C. E., Lythgoe, B., and Todd, A. R., *Nature*, 1939, **144**, 73.

¹¹ Hoffer, M., and Reichstein, T., *Nature*, 1939, **144**, 72.

¹² Oleson, J. J., Woolley, D. W., and Elvehjem, C. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **42**, 151.

They observed, further, that the pantothenic acid would not completely replace the original liver extract or crude filtrate preparations, thus showing the need for still another substance which they have called factor W. These investigators believe that the rat requires the intact pantothenic acid molecule since they could demonstrate no significant weight response in rats given beta-alanine, a constituent of pantothenic acid. Recently Unna⁴ found that a single dose of 800 γ of synthetic d-pantothenic acid produced a rapid and striking gain in weight in rats depleted of pantothenic acid. The same dose of the l-form had no significant effect.

"Hydroxypantothenic acid" [N-(alpha-hydroxy- β ,- β' -dimethylbutyryl)- β -alanine] was recently synthesized by Mitchell, Snell and Williams¹³ and was found to possess marked biological activity which varied not only with the microorganism but also with the conditions under which it was grown. Because of the variable results obtained with hydroxypantothenic acid and the concordant results obtained when concentrates from natural sources were tested for pantothenic acid, these investigators concluded that natural pantothenic acid is probably a single substance and that this hydroxypantothenic acid probably does not occur in such concentrates. Because of the striking biological activity of hydroxypantothenic acid in microorganisms, studies were undertaken to test the physiological activity of this compound in rats. The present publication reports the results of such a study.

Method. A litter of 13 rats was weaned at 35 days of age and given the following basal diet used by Elvehjem and his associates:¹² sucrose 76%; purified casein 18%; salts 4%, and corn oil 2%. In addition, each rat received 24 γ thiamin, 40 γ riboflavin, 50 γ vitamin B₆; 6 mg choline; 6 mg nicotinic acid; 6 mg vitamin C; and 200 γ vitamin K every other day and 35 mg halibut liver oil; 21 mg alpha tocopherol; and 350 mg linseed oil per week. At the end of 6 days, the 13 rats were divided into 4 groups. Group I (4 rats) served as control; Group II (3 rats) received 293 γ racemic synthetic Na pantothenate every other day; Group III (3 rats) received 720 γ racemic synthetic hydroxypantothenic acid every other day; Group IV (3 rats) received a mixture of 293 γ synthetic Na pantothenate and 720 γ synthetic hydroxypantothenic acid every other day. The study was continued over a period of 8 weeks. Weights were recorded on each animal 3 times a week.

Results. Table I shows the total increase in weight in each rat during the 8-week period of experimentation.

¹³ Mitchell, H. K., Snell, E. E., and Williams, R. J., *J. Am. Chem. Soc.*, 1940, **62**, 1791.

TABLE I.

Group I (Control)	Group II (Na pantothenate)	Group III (Hydroxypanto- thenic acid)	Group IV (Na pantothenate plus hydroxypantothenic acid)
♂ 49 g	♀ 95 g	♀ 61 g	♀ 110 g
♂ 56	♀ 89	♂ 78	♂ 78
♀ 30	♂ 121	♀ 62	♂ 115
♀ 20			

It can be seen from the data in Table I that the rats which received either synthetic Na pantothenate or synthetic hydroxypantothenic acid demonstrated a greater growth response than did control rats which received all of the known vitamins other than pantothenic or hydroxypantothenic acid. The growth response was greater in the Na pantothenate group than in the hydroxypantothenic acid group, indicating that although hydroxypantothenic acid has a stimulating effect, it is not a complete substitute for Na pantothenate in the nutrition of the rat. The two acids do not appear to supplement one another.

Summary. Rats maintained on a basal sucrose diet supplemented with vitamin B₁, riboflavin, vitamin B₆, choline, nicotinic acid, vitamin C, vitamin K, halibut liver oil, alpha tocopherol, and linseed oil exhibit a definite growth response following the addition of synthetic Na pantothenate or hydroxypantothenic acid. The growth response is greater in rats receiving Na pantothenate than it is in rats receiving hydroxypantothenic acid, indicating that Na hydroxy pantothenate is an incomplete substitute for Na pantothenate.

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Physiology of a Pure Culture of *Trichomonas vaginalis*. I: Population in Relation to pH.*

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The effect of pH upon the growth of *Trichomonas vaginalis* is probably related to the problem of clinical control of the organism

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