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Effect of Succinylsulfathiazole on the Urinary Excretion of Folic Acid by the Rabbit.*

ROBERT E. SIMPSON, B. S. SCHWEIGERT,[†] AND P. B. PEARSON.

From the Department of Biochemistry and Nutrition, Texas Agricultural Experiment Station, College Station.

Previous studies¹ showed that the growing rabbit does not require a dietary source of pantothenic acid or riboflavin when a purified diet is fed. Further, the urinary and fecal excretion of these vitamins and also of biotin greatly exceeded the intake and was not appreciably reduced when 1% of succinylsulfathiazole was included in the diet. Preliminary experiments indicated that the folic acid excretion was greatly reduced when the sulfa drug was fed; consequently these studies have been extended to obtain further information on the excretion of folic acid by rabbits receiving purified diets with and without the addition of succinylsulfathiazole.

Experimental. In the first experiment New Zealand white rabbits with an initial weight of approximately 1060 g were fed the basal ration or the basal ration plus 2% succinylsulfathiazole. Six rabbits were used in each group. The basal ration was composed of corn oil 8%, cellulose 12%, Salts IV² 4%, vitamins A and D concentrate 0.5%, cerelose to 100% and tocopherols, 2-methyl 1-4-naphthoquinone, thiamine, riboflavin, nicotinic acid, pyridoxine, Ca pantothenate, choline, inositol, biotin and para-aminobenzoic acid in adequate amounts.¹ After 3-4 weeks on experiment quantitative urine collections were made and the amount of folic acid in the urine was

determined with pteroylglutamic acid as the standard and *S. faecalis* R the test organism.³ Individual urine collections were made for 3 day periods from the 4th to the 10th week alternately for 3 of the 6 rabbits in each group. The technics used for the urine collections and preservation were described previously.¹ Other groups fed the basal ration + 2.0 mg of pteroylglutamic acid per kg of ration and the basal ration + pteroylglutamic acid and succinylsulfathiazole were included in this experiment, however the urinary excretion of folic acid was not determined for these groups.

A second experiment was carried out with 8 rabbits fed the basal ration and 8 fed the basal ration plus succinylsulfathiazole. The initial weight of the rabbits averaged 1720 g. Urine collections were again made and the folic acid excretion determined. The results obtained for both experiments are shown in Table I.

Results and Discussion. The rabbits receiving the basal ration without added sulfa drug grew at a normal rate. The rate of gain for other groups which received 2.0 mg of pteroylglutamic acid per kg of ration was not increased. The rate of gain has been shown to increase when liver extract is added.⁴ The addition of 2% succinylsulfathiazole to the ration markedly reduced the rate of gain of most rabbits, however the rabbits with a larger initial weight, particularly in the second experiment, were not severely retarded in weight gains. The rates of gain of the control groups included in the first experiment that received pteroylglutamic acid with or without the sulfa drug were normal.

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[†] Present address: Division of Biochemistry and Nutrition, American Meat Institute Foundation, University of Chicago.

¹ Oleese, O., Pearson, P. B., and Schweigert, B. S., *J. Nutrition*, 1948, **35**, 577.

² Hegsted, D. M., Mills, R. C., Elvehjem, C. A., and Hart, E. B., *J. Biol. Chem.*, 1941, **138**, 459.

³ Teply, L. J., and Elvehjem, C. A., *J. Biol. Chem.*, 1945, **157**, 303.

⁴ Kunkel, H. O., Simpson, R. E., Pearson, P. B., Oleese, O., and Schweigert, B. S., *Proc. Soc. Exp. Biol. and Med.*, 1948, **68**, 122.

TABLE I.
Effect of Ingesting Succinylsulfathiazole on Urinary Excretion of Folic Acid by the Rabbit.*
(μg excreted per rabbit per day).

Dietary regimen	Weeks on experiment						
	4	5	6	7	8	9	10
Exp. I							
Basal	2.3	1.5	2.6	3.6	10.9	4.8	8.9
Basal + S.S.	1.1	0.5	1.6	1.8	2.2	1.9	2.4
Exp. II							
Basal	2.6	3.0	7.8	16.0	—	3.8	3.4
Basal + S.S.	1.0	1.0	2.5	3.7	—	0.4	0.5

* The values are averages of 3 individual 3-day collections for the first experiment and of 6 individual collections for the second experiment.

The addition of 2% of succinylsulfathiazole markedly reduced the urinary excretion of folic acid active compounds. This effect was evident by the 4th week and although the excretion of folic acid remained at a low level for the succinylsulfathiazole group, a considerable increase in the apparent synthesis of folic acid was observed for the basal group, particularly from the 7th to 10th weeks. Although accurate measurements of folic acid in the ration were not achieved due to the low level, the estimated dietary intake of 1 μg per day approximated the amount excreted by the sulfa fed group and was much lower than the amount excreted by the basal group. It may be concluded therefore that the rabbit is capable of synthesizing sufficient folic acid, as well as pantothenic acid, riboflavin, and biotin, presumably by intestinal microorganisms to meet its needs and that the apparent synthesis of folic acid can be

markedly reduced by the inclusion of 2% succinylsulfathiazole in the ration.

Other tests showed that the inclusion of succinylsulfathiazole in the ration did not reduce the hemoglobin level of the blood. Rabbit blood was found to contain folic acid conjugase;⁵ however the level of apparent free folic acid in blood was very low (<1.0-4.0 millimicrograms per ml) and the data obtained do not permit an accurate evaluation of the folic acid blood levels of the groups receiving and not receiving the sulfa drug.

Summary. The urinary excretion of folic acid by rabbits fed purified diets with or without the addition of succinylsulfathiazole was studied. The inclusion of the drug markedly reduced the urinary excretion of folic acid. This effect was evident from the 4th to the 10th week of the experiments.

⁵ Simpson, R. E., and Schweigert, B. S., *Arch. Biochem.*, 1949, **20**, 32.

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Dissociation Among Lancefield's Group "B" Streptococci of Human and Bovine Origin.*

A. POMALES-LEBRÓN AND P. MORALES-OTERO.

From the Department of Bacteriology, School of Tropical Medicine, San Juan, Puerto Rico.

One hundred and thirty bovine and 26

* This investigation was conducted with the cooperation of the following institutions: San Juan City Hospital, Bayamón District Hospital and the Veterans Hospital at San Patricio.

human strains of Lancefield's group "B" streptococci were studied within one month after isolation.

Primary isolations were made on beef heart infusion agar (Difco) which contained 3%