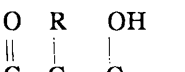
tion and the cyanosis might have resulted from intravascular hemolysis of red cells caused by the drugs. However, as shown by the results of hypotonic fragility studies, the compounds were not in themselves hemolytic.

It has been postulated(4) that the configuration  , present in previously studied active naphthoquinone, hydroxycoumarin, and indandione(5) derivatives, is necessary for antivitamin K activity. The results obtained in this study show that in defining the moiety necessary for antivitamin K activity, at least in naphthoquinone derivatives, one must specify the nature of the substituent R attached to the 2 position. Furthermore, the findings of Seeler(6) and Mushett (7) with 2-sulfanilamidoquinoxaline demonstrate that certain compounds with other configurations are active in antagonizing vitamin K.

Summary. Three phthiocol derivatives containing a side chain with a basic nitrogen have been examined for hemorrhagic activity and found to be inactive. The bearing of these findings on the structural configuration necessary for antivitamin K activity has been discussed.

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Received February 23, 1950. P.S.E.B.M., 1950, v73.

Action of N-Benzyl-2-furamide in Experimental Tuberculosis. Comparison with a Sulfone and Streptomycin. (17745)

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In a review of the chemotherapy of tuberculosis Rist(1) cites the work of Shpanir and associates(2) suggesting an antitubercular activity for the benzylamide of a furan carboxylic acid. The moderate activity of the sulfones in experimental tuberculosis and their ability to potentiate the action of streptomycin(3,4) prompted a search for other possible leads. Accordingly an experiment was set up to determine the potential antitubercular possibilities of this furan derivative.

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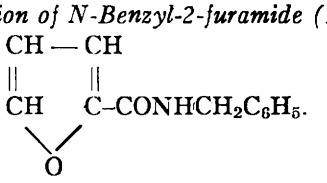
Preparation of N-Benzyl-2-furamide (NBF)–  .

This compound, reported by Bowen and Smith(5), was synthesized by the action of furoyl chloride upon benzylamine in aqueous solution, with the addition of sodium hydroxide solution at intervals in order to neutralize the hydrochloric acid formed. The reaction was complete after 6 hours. After recrystallization from alcohol, the colorless crystals melted at 112-113°. This compound is only slightly soluble in water.

Toxicity. NBF was tolerated in guinea pigs in single doses of 0.5 g/kg when given orally

5. Bowen, C. V., and Smith, L. E., *J. Am. Chem. Soc.*, 1940, v62, 3522.

TABLE I.
Toxicity of N-Benzyl-2-furamide in Guinea Pigs. Oral Administration of Aqueous Suspension with Gum Acacia.

Dose, g/kg	No. used	No. died	Remarks
2.0	5	5	All died in 1-4 days. Labored respiration and progressive depression
1.5	5	2	Died in 1-3 days
1.0	5	1	Died in 3 days
0.5	5	0	

TABLE II.
Activity of N-Benzyl-2-furamide (NBF) in Experimental Guinea Pig Tuberculosis as Compared with That of a Sulfone (GLS) and Streptomycin (SM). All animals infected with 0.5 mg H37Rv Intraperitoneally.

Group	Treatment	No. used	Avg wt gain, g	No. died	T.B. index* Range	T.B. index* Avg	Chemotherapeutic effectiveness†
1	Controls	9	77	5	8–20	14.4	
2	SM 20 mg/kg	10	285	0	±–4	1.5	9.6
3	SM 40 mg/kg	10	259	0	0– 2	0.9	16.0
4	NBF 250-500 mg/kg	9	34	7	5–19	12.2	1.2
5	GLS 100 mg/kg	10	230	1	1–11	5.0	2.9
6	SM 20 mg/kg + NBF 250-500 mg/kg	7	234	0	0– 3	1.1	13.1
7	SM 20 mg/kg + GLS 100 mg/kg	6	220	0	0– 2	0.7	20.6

* Extent of tuberculous involvement, rated as previously described. See Ref. 6.
† Average T.B. index of controls/treated.

in aqueous suspension with gum acacia. Larger doses killed some or all of the animals in 1-3 days as shown in Table I. Visceral congestion, mottling of the liver, pleural effusion and ascites were seen at autopsy. The compound was administered to the limits of tolerance, in daily doses of 250-500 mg/kg, in the therapeutic tests described below.

Antitubercular Activity. A series of male guinea pigs weighing about 300 g were inoculated intraperitoneally with 1 cc of a homogeneous suspension of tubercle bacilli containing 0.5 mg, moist weight of the human strain H37Rv. They were divided into 7 groups as follows:

1. 9 controls
2. 10 treated with 20 mg/kg streptomycin intramuscularly once daily
3. 10 treated with 40 mg/kg streptomycin as above
4. 9 treated with 250-500 mg/kg NBF orally once daily
5. 10 treated with 100 mg/kg galacturonic acid derivative of 4,4′-diaminodiphenylsulfone (GLS) orally once daily
6. 7 treated with 20 mg/kg streptomycin intramuscularly and 250-500 mg/kg NBF orally, each once daily.
7. 6 treated with 20 mg/kg streptomycin intramuscularly and 100 mg/kg GLS orally each once daily.

All treatments were begun the day after infection and continued 5 days a week for 10 weeks. At the end of the experimental period all the survivors were killed with chloroform, autopsied and the extent of tuberculous involvement rated as previously described(6).

The results of this are summarized in Table II. The data indicate practically no activity for the furan derivative. The sulfone on the other hand, which was used for comparison, had a moderately good activity, almost one third that of streptomycin, at the dose levels employed. It should be mentioned that the activity of the sulfone in the present test was almost identical with that previously found(7).

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7. Smith, M. I., McClosky, W. T., and Jackson, E. L., *Am. Rev. Tuberc.*, 1947, v55, 366.

When used in combination with streptomycin the furan derivative showed only a slight degree of potentiation (chemotherapeutic effectiveness of 13.1 as against 9.6 + 1.2 or 10.8), while the sulfone showed a high degree of potentiation. The chemotherapeutic effectiveness of combined therapy with streptomycin and the sulfone was 20.6 as against 9.6 + 2.9 or 12.5, the sum of the effects of the two drugs. It should be noted that the chemotherapeutic effectiveness of sulfone-streptomycin combined therapy was somewhat greater than that of the double dose of streptomycin.

Comments and conclusions. The favorable results reported by Shpanir for the benzyl furamide were based on experiments in mice. Though the mouse test is currently in use in several laboratories for screening of compounds for possible antitubercular activity we are not impressed with it as a satisfactory test object(8). It is possible that the present results are at variance with those of Shpanir on account of species differences.

N-Benzyl-2-furamide has no appreciable activity in experimental tuberculosis in guinea pigs. So far the sulfones alone, next to streptomycin, have been demonstrated to have a definitely suppressive effect on this disease.

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Received February 24, 1950. P.S.E.B.M., 1950, v73.

Oral Treatment of Pernicious Anemia with Swine Duodenal Mucosa and Vitamin B_{12}. (17746)

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Since the initial report by West(1) there has been ample evidence that the parenteral administration of as little as 1-2 μg of vitamin B_{12} daily to pernicious anemia patients in relapse is followed by reticulocytosis, rise in hemoglobin and erythrocytes, and clinical remission(2-6). The minimal effective oral daily dose lies between 75 and 150 μg(7,8). However, the oral administration of gastric juice from a normal person with 5 to 10 μg of vitamin B_{12} results in satisfactory hematologic and clinical response(9,10). More recently Bethell has shown that the ingestion of an extract of desiccated swine duodenal mucosa and 5 μg of vitamin B_{12} daily will induce a similar reaction(11). It is the purpose of this report to present additional data confirming this latter observation.

Two patients with typical Addisonian pernicious anemia in relapse were treated with daily oral doses of 2 g of an aqueous extract of swine duodenal mucosa and 10 μg of vita-

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