is apparently different, and so correlation between these results and human reactions must be carefully analyzed. These data would suggest that monkeys should be used for animal experimentation on this complex system.

Summary. An euglobulin fraction of serum or plasma from animals and man contains a proteolytic precursor or active enzyme. The activation pattern of this enzyme precursor in man and monkeys is different from that of dogs, guinea pigs and rabbits.

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Absence of Hemorrhage Inducing Activity in Phthiocol Derivatives with a Basic Nitrogen in Side Chain. (17744)

CARL C. SMITH.

From the Christ Hospital Institute of Medical Research, Cincinnati, Ohio.

In previous reports(1,2) it was shown that 3-hydroxy-1,4-naphthoquinone derivatives, substituted in the 2 position with a hydrocarbon chain of 6 or more carbon atoms, induced a hemorrhagic syndrome in the rat. This syndrome, characterized by a marked hypoprothrombinemia, could be prevented by administration of vitamin K (2-methyl-1,4-naphthoquinone) or K_1 (2-methyl-3-phytyl-1, 4-naphthoquinone), the latter being more active than the synthetic compound. From these findings it was postulated that these phthiocol analogues competed with vitamin K in the processes concerned with prothrombin production.

More recently we have examined 3 phthiocol derivatives* with a basic nitrogen atom in the side chain attached in the 2 position of the naphthoquinone. These derivatives were A 223, 2 - (piperidinomethyl) - 3 - hydroxy-1,4-naphthoquinone, A 1506, 2-(n-butylaminomethyl)-3-hydroxy-1,4-naphthoquinone, and A 1507, 2-(n-decylaminomethyl)-3-hydroxy-1,4-naphthoquinone.

The technics employed in the present study were the same as those used previously(1,2). Male rats, 4-5 weeks old, Sprague-Dawley strain, were used and were fed Purina Dog Chow checkers and tap water *ad libitum*. The drugs, suspended in olive oil, were administered once daily via stomach tube in doses of 400, 800, and 1600 mg/kg. Six rats were given each drug level and the treatments were given for 10 days if the rats survived that long. Prothrombin time determinations(3) were performed on whole blood obtained by cardiac puncture either at the end of the treatment period or when a rat became moribund. At the end of the treatment period all rats were sacrificed and necropsies were performed.

Compound A 223 was found to be about 4 times as toxic as A 1506 and considerably more than 4 times as toxic as A 1507. Two of the 6 rats receiving 400 mg/kg A 223 succumbed; larger doses were uniformly fatal. A 1506 retarded growth at a dose of 800 mg/kg and was lethal to 4 of 6 rats at 1600 mg/kg. No toxicity other than a slight retardation of growth was noted with A 1507 even when doses of 3200 mg/kg were administered. The rats intoxicated with A 223 or A 1506 were usually pale and cyanotic. There was no evidence, however, of the hemorrhagic syndrome encountered in the previous studies. Prothrombin times of both the treated rats and the control animals were all within or close to the normal range (15-18 seconds). Occasionally in the rats receiving A 223 or A 1506 splenic enlargement and a brownish pigmentation of the lungs, heart, and skin were observed at necropsy. It was thought that this pigmenta-

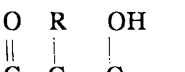
1. Smith, C. C., Fradkin, R., and Lackey, M. D., PROC. SOC. EXP. BIOL. AND MED., 1946, v61, 398.

2. Smith, C. C., PROC. SOC. EXP. BIOL. AND MED., 1947, v64, 45.

* These compounds were obtained from Dr. M. T. Leffler, Abbott Laboratories.

3. Kato, K., *Am. J. Clin. Path.*, 1940, v10, 147.

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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5. Kabat, H., Stohlman, E. F., and Smith, M. I., *J. Pharm. and Exp. Therap.*, 1944, v80, 160.

6. Seeler, A. O., Mushett, C. W., Graessle, O., and Silber, R. H., *J. Pharm. and Exp. Therap.*, 1944, v82, 357.

7. Mushett, C. W., and Seeler, A. O., *J. Pharm. and Exp. Therap.*, 1947, v91, 84.

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

M. I. SMITH, HUGO BAUER, Y. T. CHANG,* AND H. FRIEDLANDER.
From the National Institutes of Health, Bethesda, Md.

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.

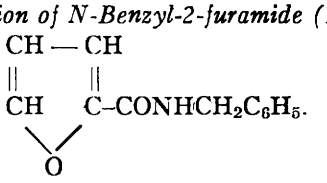
* N.I.H. Fellow.

1. Rist, N., *Bibliotheca Tuberculosea, Suppl. Schw. Z. f. Tub.*, 1948, 101.

2. Shpanir, F. L., and Chertkova, E. L., *Probl. Tuberk.*, 1944, v22, 9.

3. Smith, M. I., McClosky, W. T., Jackson, E. L., and Bauer, H., PROC. SOC. EXP. BIOL. AND MED., 1947, v64, 261.

4. Smith, M. I., Jackson, E. L., and Bauer, H., *Ann. N. Y. Acad. of Sciences*, 1949, v52, 704.

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.