

A detailed report of our work will be presented in the future.

We acknowledge gratefully valuable suggestions of Dr. H. Gilman and Dr. F. B. LaForge. We are also indebted to Merck & Co., Inc., for generously furnishing us with a supply of the pyrimidine derivative used in this work. The analytical work was carried out by Dr. Carl Tiedcke of New York City.

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VITAMIN K POTENCIES OF SYNTHETIC COMPOUNDS

Sir:

In view of the failure of the absorption of many patients in which vitamin K therapy is highly desirable, we have been examining various compounds which could be administered intravenously in aqueous solution. The most active compound found is 1,4-dihydroxy-2-methylnaphthalene which has a potency of approximately 1000 Thayer-Doisy units per milligram. It can be prepared readily by the reduction of the highly potent 2-methyl-1,4-naphthoquinone. Since this preparation is soluble in dilute alkali and has a high degree of potency (approximately equal to the potency of 2-methyl-1,4-naphthoquinone), it seems that this compound may prove very important for intravenous vitamin K therapy.

Supplementing our previous preliminary report [THIS JOURNAL, 61, 1932 (1939)], we have reassayed several quinones to determine their optimum potency values. Except for 2-methyl-1,4-naphthoquinone, these more recent data agree with our previous findings. The assay of this compound was carried out by the Thayer-Doisy method, making a concurrent test, at six, eighteen and seventy-two hours. The standard was also run at varying levels at the same time for each series. The data are given in Table I. The details as to the method of feeding, care of the chicks, length of test period, manner of bleeding, etc., were essentially the same as described previously.

TABLE I

Assay period	Thayer-Doisy units per mg.
6 hours	1110
18 hours	970
72 hours	1070
Average	1050

The potency of 2-methyl-1,4-naphthoquinone (Thayer-Doisy units) agrees with the value previously assigned to the natural K₁, namely, 1000 units per milligram [*Proc. Soc. Exp. Biol. Med.*, 41, 194 (1939)]. These results also confirm the findings of Ansbacher and Fernholz [THIS JOURNAL, 61, 1932 (1939)].

Incidentally, in view of these observations and the lack at this time of a suitable standard, it is suggested that 2-methyl-1,4-naphthoquinone should be adopted as a basic standard for the assay of vitamin K. This compound has the desirable qualities of a standard in that it can be obtained readily in a satisfactory state of purity, has a definite melting point for characterization, and when protected from excessive exposure to light is relatively stable. The unit could then be defined in the terms used by the League of Nations committee as the specific vitamin K activity of one microgram of pure 2-methyl-1,4-naphthoquinone.

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RECEIVED AUGUST 21, 1939

ANTIHEMORRHAGIC ACTIVITY OF SIMPLE COMPOUNDS

Sir:

In connection with our investigation of vitamin K, we have tested recently a large number of derivatives of α -naphthoquinone, many of which have been prepared and reported by Professor Fieser and his collaborators¹ and some of which were synthesized in this Laboratory. At this time we wish to report our findings of the antihemorrhagic activity of 2-methyl-1,4-naphthoquinone and of some other related substances of significance.

One of the first quinones we assayed was 2-methylnaphthoquinone and, because it did not appear at that time to be as active as 2,3-dimethyl-1,4-naphthoquinone,¹ we did not determine its minimum dose.

Following the appearance of the extremely interesting report of Ansbacher and Fernholz,² we reinvestigated the activity of 2-methyl-1,4-naphthoquinone, and we are now in complete agreement with them.

(1) Fieser, *et al.*, THIS JOURNAL, 61, 1925, 1926, 2206 (1939).

(2) Ansbacher and Fernholz, *ibid.*, 61, 1924 (1939).