

## LETTERS TO THE EDITORS

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## A New Vitamin A

AN earlier publication<sup>1</sup> presented evidence which indicated that fish liver oils contain a substance (or substances) which has vitamin A activity but differs in properties from the vitamin A (here designated A<sub>1</sub>) previously obtained in crystalline form<sup>2</sup>. Subsequent research has revealed that the newly recognized compound occurs in fish liver oils in substantial amounts, being responsible for approximately one third of their total vitamin A potency.

We have succeeded in isolating the vitamer\* from fish liver oils in pure form. It crystallizes as light yellow needles (m.p. 59–60°) which contrast with the yellow prisms (m.p. 62–64°) of vitamin A<sub>1</sub>. It has an absorption maximum at 328 mμ ( $E_{1\text{ cm}}^{1\text{ per cent}} = 1675$ ) while vitamin A<sub>1</sub> has its absorption maximum at 325 mμ ( $E_{1\text{ cm}}^{1\text{ per cent}} = 1750$ ). It is an alcohol which forms a red anthraquinone carboxylate (m.p. 130–131°), while vitamin A<sub>1</sub> yields a corresponding ester which is yellow (m.p. 123–124°). By treatment with alcoholic hydrochloric acid it forms the same anhydro compound (m.p. 76–77°)<sup>3</sup> as vitamin A<sub>1</sub>, but the reaction proceeds much more slowly. It is more stable to atmospheric oxidation than vitamin A<sub>1</sub>.

The constitution of the new vitamer has not yet been definitely established. The available evidence, however, suggests that it may be a geometrical isomer of vitamin A<sub>1</sub> differing in the *cis-trans* configuration at the double bond nearest the hydroxyl group.

A method has been developed for estimating the percentage of the new substance in fish liver oils and concentrates. This is based on the observation that maleic anhydride reacts more slowly with it in benzene solution than with vitamin A<sub>1</sub>. Analyses of samples of soupfin shark and dogfish liver oil showed that 30 per cent and 33 per cent, respectively, of the vitamin A was the newly recognized compound.

A second method of estimation of the vitamer depends on the fact that it forms the anhydro compound on treatment with alcoholic hydrochloric acid much more slowly than vitamin A<sub>1</sub>. The procedure is less useful than the one just described because it must be carried out on the saponified fish liver oil or concentrate.

A preliminary bio-assay on the new compound has indicated that its potency is nearly the same in kind and magnitude as that of vitamin A<sub>1</sub>. More extensive assays are in progress.

The recognition that the vitamin A activity of fish liver oils is due to at least two different substances emphasizes the need for an improved system of nomenclature. The term 'axerophthol' proposed by Karrer for vitamin A<sub>1</sub> has not gained general usage and moreover establishes no basis for naming newly discovered vitamers. The use of subscripts is also unsatisfactory. For example, while the vitamin A<sub>2</sub> found in the liver oils from freshwater fish possesses curative powers for the vitamin A-deficiency

syndrome, it probably has a basically different structural formula than vitamin A<sub>1</sub>.

We have consulted various authorities in the United States and have suggested that the A-vitamins in fish liver oils be named from the genus of fish in which they were first found or in which they occur in concentrated form. Suggested terms were 'gadol' for vitamin A<sub>1</sub> from *Gadus*, the cod; and 'galol' for the new vitamer from *Galidæ*, the shark. If other A vitamins are discovered in the future they could be named readily by this system, which is now being considered by the Committee on Biochemical Nomenclature of the U.S. National Research Council.

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<sup>1</sup> Baxter, J. G., Harris, P. L., Hickman, K. C. D., and Robeson, C. D., *J. Biol. Chem.*, **141**, 991 (1941).

<sup>2</sup> Baxter, J. G., and Robeson, C. D., *J. Amer. Chem. Soc.*, **64**, 2411 (1942).

<sup>3</sup> Shantz, E. M., Cawley, J. D., and Embree, N. D., *J. Amer. Chem. Soc.*, **65**, 901 (1943).

Antibiotic Action of an *Aspergillus* Strain against *Mycobacterium tuberculosis*\*

IN the course of investigations on the growth conditions of *Mycobacterium tuberculosis*<sup>1</sup>, we have observed that contamination by an *Aspergillus* strain of cultures of *M. tuberculosis* human and bovine type resulted in a distinct inhibition of growth. Systematic experiments founded on this observation led to the preparation of filtrates from pure cultures of the mould, which were active against *M. tuberculosis* human and bovine type. A preliminary report of our results was presented to the Swedish National Society against Tuberculosis on October 1, 1943. In view of a recent communication by M. A. Soltys<sup>2</sup>, we wish to report briefly our findings.

Our *Aspergillus* strain (the identification of which is not yet completed), when grown on a synthetic medium containing iron-, sodium- and magnesium-salts, glycerine and certain nitrogenous substances, such as asparagine, at pH 7.2 (phosphate buffer) and at 37° C., produces an antibiotic, which inhibits the growth of *M. tuberculosis* and of *Staphylococcus aureus*. No antibiotic is produced, when the mould is grown on a Czapek-Dox medium. Soltys states that his 'aspergillin' is inactive against *Staphylococcus aureus*; thus, the antibiotic present in our culture filtrates may be different from 'aspergillin'. The chemical properties so far investigated point to the non-identity of our product with the known antibiotics isolated from aspergillus cultures, such as glyotoxin, helvolic acid or patulin. A detailed account of these investigations will be published elsewhere.

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\* Swed. Pat. Appl. 7748/43 (6 Nov., 1943).

<sup>1</sup> Kallós, P., "Beitr. zur Immunbiologie der Tuberkulose" (Stockholm: H. W. Tullberg, 1941).

<sup>2</sup> Soltys, M. A., *Nature*, **154**, 550 (1944).

\* The word 'vitamer' was introduced simultaneously by Dean Burke and associates of the National Cancer Institute and workers at Distillation Products, Inc., to indicate two or more substances which have the same ability to cure a single deficiency syndrome.