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Note

Choleic Acid Complexes of Vitamins K_1 and K_3

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In 1939 Almquist and Klose[1] reported the isolation of vitamin K, as a choleic acid complex from alfalfa concentrates as a slightly yellow crystalline substance, m.p. 186–187°, which gave a colour-reaction with sodium methoxide and contained about 10 per cent of the vitamin, but they reported neither analyses nor the spectrum of the product.

Additional interest in the complex results because vitamin K is only absorbed in the presence of bile salts, especially desoxycholic acid.[2] The complex was found to be highly active in restoring the normal clotting time in deficient chicks;[1] yet, it was only partially successful in rising the prothrombin level in bile fistula rats.[3]

We have now observed that vitamin K_1—which is known to occur in alfalfa—easily forms a choleic acid complex, different from that described by Almquist and Klose. It is also a pale yellow solid, which gives the colour reaction with sodium methoxide, but melts sharply at 167°. The spectrum in ethanol is identical to that of vitamin K_1; this observation was applied for the determination of the coordination number[4] which was found to be eight.

Neither by careful fractional crystallization nor by altering the ratio of vitamin to bile acid, nor by closely following the procedure of Almquist and Klose could a choleic acid complex other than the one melting at 167° be obtained.

Certain preparations of alfalfa concentrates appear to contain more than one substance with vitamin K activity.[5,6] Yet from their purest concentrates Almquist and Klose could not obtain any other choleic acid except the one melting at 186–187°. With cruder concentrates they obtained inactive fractions in addition

to the active fraction. None of these fractions melted near 167°.*

2-Methyl-1,4-naphthoquinone (menadione, vitamin K_3) forms a dicholeic acid complex† which is yellow and melts at 173–174°.

Preliminary experiments indicate that oral administration of the complexes of vitamin K_1 or vitamin K_3 with choleic acid are effective in varying prothrombin and factor VII values from low levels.

Experimental

Vitamin K_1/choleic acid complex. The vitamin, fairly pure by spectrophotometric assay, and 6 to 11 times its weight of desoxycholic acid (m.p. 169·5–172·5°; $[\alpha]_D$ in 95 per cent ethyl alcohol, +54°) were dissolved in the minimum amount of almost boiling ethyl alcohol. The solid which separates on cooling was collected.

Anal.[4] Calcd. for vitamin K_1 for an octacholeic acid complex: 12·54. Found: 12·7; 12·8. The complex should not be recrystallized from ethyl alcohol. It is practically insoluble in bicarbonate solution.

Vitamin K_3/choleic acid complex. The preparation is analogous to that of the vitamin K_1 complex except that somewhat more definite proportions are required. Good results were obtained using the vitamin (1 g), the acid (8·1 g) and ethanol (30 ml).

Anal.[4] Calcd. for vitamin K_3 for a dicholeic acid complex: 17·9. Found: 17·6, 17·7. The complex is slightly soluble in bicarbonate solution.

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* The product obtained by Almquist and Klose was not the choleic acid complex of vitamin K_1 oxide. This complex, which has now been prepared and is being further investigated, melts at 165° and in accordance with expectation is colourless and does not give the colour reaction with sodium methoxide.

† We have also attempted the preparation of the complexes of α-tocopherol and vitamin D_2 with choleic acid but the above conditions were not successful.

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