

controlled observations on large litters sired by heterozygous males seem particularly attractive.

In the litter described, the pups had suckled for about two hours before the first blood samples were drawn. Dopositive pups in three subsequent litters were similarly affected, but examinations of the blood before and after suckling revealed that most, if not all, of the Do-antibody was acquired from the dams' milk.

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The Antithyroid Factor of Yellow Turnip¹

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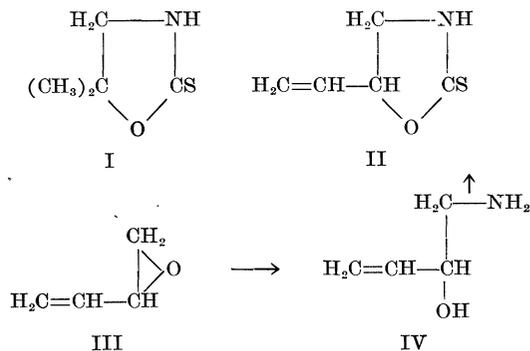
It has been well established that goiter may be induced in laboratory animals by diets of certain vegetables such as cabbage, turnip, or rape. A recent study (2) of the antithyroid effect of various foods in man disclosed marked activity in the yellow turnip or rutabaga, *Brassica napobrassica*. This antithyroid principle has now been isolated in crystalline form and its structure determined.

The purification of the goitrogen was controlled by antithyroid assay of crude preparations in the rat, and later by measurement of the ultraviolet absorption spectrum. The active substance was released from ground rutabaga root by extraction with cold water, and concentrated by appropriate distribution between ether and alkaline buffers. The concentrates so prepared could be crystallized directly from ether with the aid of seed crystals, which were originally obtained from material that had been further purified by distillation in high vacuum and chromatographic adsorption on alumina. The active principle was isolated in a yield of 0.2 g/kg of root as colorless crystals of formula C_5H_7ONS , mp 50° , $[\alpha]_D^{25} - 71^\circ$ (2% methanol solution). The same substance was obtained from the root of white turnip, and in larger quantities (1-8 g/kg) from the seeds of rutabaga, white turnip, cabbage, kale, and rape. Its antithyroid activity in man approximately equals that of 6-*n*-propylthiouracil.

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Since no pure chemical degradation product could be obtained from the goitrogen, its structure was deduced largely from physical evidence. The compound in aqueous solution was found to be a weak acid (pK_a 10.5) and to have an intense ultraviolet absorption maximum at $240 m\mu$ and $\log \epsilon$ 4.24, which was shifted by alkali to $232 m\mu$, $\log \epsilon$ 4.06. In these properties it closely resembled 5,5-dimethyl-2-thiooxazolidone (formula I), a natural product (3) of similar composition. Furthermore, the infrared absorption spectrum of the unknown in chloroform solution exhibited a system of bands at 2.9μ , 3.15μ , 6.6μ (inflected at 6.5μ), and 8.6μ , which was found to be highly characteristic of 2-thiooxazolidones, and contained two bands at 10.17μ and 10.85μ , indicating the presence of a vinyl group (1). Coupled with the absence of terminal methyl groups, these facts required that the rutabaga goitrogen have the structure of a vinylthiooxazolidone. The observation that treatment of the substance with boiling 4N HCl destroyed optical activity without liberating ammonia strongly suggested the attachment of the oxygen rather than the nitrogen atom to the allylic center of asymmetry. Therefore, the antithyroid factor of rutabaga was considered to be L-5-vinyl-2-thiooxazolidone (formula II).



The assigned formula was confirmed by synthesis. Reaction of butadiene 1,2-dioxide (formula III) (4) with ammonia produced a mixture from which a pure aminoalcohol, in all probability L-1-amino-3-buten-2-ol (formula IV), was separated as its acid oxalate, mp 131° . Conversion of this aminoalcohol to the dithiocarbamate with carbon disulfide and alkali, followed by cyclization with lead nitrate, furnished DL-5-vinyl-2-thiooxazolidone, mp 63° , which had the same infrared spectrum as the rutabaga factor. L-1-Amino-3-buten-2-ol, obtained by resolution of the racemic aminoalcohol with D- α -bromocamphor- π -sulfuric acid, was similarly transformed into synthetic L-5-vinyl-2-thiooxazolidone, identical with the natural product.

References

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