The result shows that compounds I and II are comparable to neomercazole as goitrogens on the basis of the above test. It has since been observed that I and II are *orally* active, do not affect the body weight and have no adverse effect on the liver, kidney or other vital organs of the treated animals, at the above mentioned doses. None of these compounds has any effect on serum cholesterol. Compound II is relatively less toxic and could be administered orally to mice at a dose of 600 mg/kg without any lethal effect. These and other related studies will be published elsewhere in detail[2].

Further researches on compound II and its possible derivatives are in progress with a view to exploring its therapeutic use.

*Zusammenfassung.* Es wurden an Ratten einige 1-Alkylimidazolidin-2-thione auf ihre thyreostatische Wirkung geprüft. Das 1-Äthyl und das 1-Isopropylderivat sind in ihrer Wirkung mit Neomercazol vergleichbar.

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## The Effect of α-Ethyl-Thioisonicotinamide on Adrenal Cholesterol and Ascorbic Acid in Rats

Stimulatory effect on adrenal cortex was observed after administration of some antituberculotics in man and in experimental animals[1-4]. The depletion of adrenal ascorbic acid and cholesterol and the increased level of blood 17-hydroxycorticosteroids in experimental animals were found after high doses of isoniazid and *p*-aminosalicylic acid[2-4]. On the other hand, a mild stimulatory effect of pyrazinamide in this respect was seen only at the beginning of the treatment[5]. We were therefore interested to find out if adrenal cholesterol and ascorbic acid concentration could be influenced by α-ethyl-thioisonicotinamide (ethionamide).

In these experiments male rats weighing 130–140 g were used. Ethionamide was administered *per os* in the dose of 300 mg/kg in water solution for a period of 3 and 7 days. Control animals received only water. The animals were sacrificed 3 h after the last dose. Right adrenals were then preparated, weighed and homogenized and cholesterol determined by the method of HENLEY[6]. Ascorbic acid was estimated in left adrenals by the method of ROE and KUETHER[7] modified by BRÜGGEMAN[8].

Table I. Effects of orally administered 300 mg ethionamide/kg on adrenal cholesterol in rats

| Group[a] | Cholesterol µg/100 mg | SD | SE | | % | Weight of adrenals mg |
|---|---|---|---|---|---|---|
| Control | 7006 | 2120 | 670 | $P < 0.01$ | −69 | 21.0 |
| 3 days 1314 Th[b] | 2159 | 732 | 231 | | | 27.4 |
| Control | 6978 | 1020 | 320 | $P < 0.01$ | −23 | 22.1 |
| 7 days 1314 Th | 5357 | 807 | 254 | | | 26.3 |

[a] In each group 10 animals were used
[b] 1314 Th = ethionamide

Table II. Effects of orally administered 300 mg ethionamide/kg on adrenal ascorbic acid in rats

| Group[a] | Ascorbic acid µg/100 mg | SD | SE | | % | Weight of adrenals mg |
|---|---|---|---|---|---|---|
| Control | 560 | 74 | 23 | $P < 0.01$ | −36 | 22.5 |
| 3 days 1314 Th | 361 | 93 | 29 | | | 28.8 |
| Control | 552 | 66 | 21 | $P > 0.1$ | −11 | 23.3 |
| 7 days 1314 Th | 491 | 108 | 34 | | | 27.5 |

[a] In each group 10 animals were used

Effects of ethionamide on adrenal cholesterol and ascorbic acid are summarized in Table I and II. As shown in Table I, three days administration of ethionamide resulted in 69% decrease of adrenal cholesterol concentration. Ethionamide administered for seven days caused 23% decrease of cholesterol. The weight of right adrenals increased from 21.0 mg to 27.4 mg on the third day and from 22.1 mg to 26.3 mg on the seventh day.

In Table II the ascorbic acid level in the left adrenals may be seen. Following the three days treatment with ethionamide, the mean values of ascorbic acid decreased by 36%. The 11% diminution in adrenal ascorbic acid concentration observed on the seventh day was not significant. The weight of left adrenal increased from 22.5 to 28.8 mg on the third day and from 23.3 to 27.5 mg on the seventh day.

It can be concluded that ethionamide administration in the dose of 300 mg/kg for a period of 3 and 7 days resulted in enlargement of the adrenals and in marked depletion of adrenal cholesterol and ascorbic acid in rats. The level of adrenal cholesterol decreased two-fold when compared with the decrease of ascorbic acid. Ethionamide exerted a lesser effect on adrenals on the seventh day of administration. The diminution of adrenal cholesterol and ascorbic acid, and ascorbic acid concentrations, in rats may be considered as indicative of a stimulatory effect of ethionamide on adrenal function.

*Zusammenfassung.* Bei Ratten wurde der Einfluss von α-Äthylthioisonicotinsäureamid (3 und 7 Tage, 300 mg/kg täglich) auf die Nebennieren verfolgt. Erhöhung des Organgewichtes sowie Herabsetzung des Ascorbinsäure- und Cholesteringehaltes wird festgestellt.

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