the pancreas. However the pancreatic values were more than twice as high as those in the liver, 59 ± 5.

Discussion. It appeared from previous studies, that the pancreatic islet tissue of *Cottus quadricornis* L. had its own characteristic distribution pattern for the amino acids formed *in vitro* from glucose[4]. The formation in the islet tissue of relatively large amounts of glutamic acid, its amide glutamine, and aspartic acid might follow from a particularly intensive transamination with transfer of amino groups to the corresponding α- ketoacids, which are important intermediates in the tricarboxylic cycle. The present determinations of the GOT and GPT activities confirm this supposition. The endocrine part of the pancreas was not only especially rich in GPT, but the activity of this enzyme was also probably higher than in the liver, which is known to be a rich source of both GPT and GOT[7-9]. While no differences were observed for GOT between the endocrine and exocrine parts of the pancreas, the pancreatic levels of this enzyme amounted to nearly half that of the liver. In the pig, for example, the concentration of GOT was about 15 times higher in the liver than in the pancreas[10].

It is worthy of note that the level of OCT was higher in the two parts of the pancreas than in the liver. During this transferase reaction citrulline is formed from ornithine and carbamylphosphate, which represents a step in mammalian urea synthesis that is known to take place in the liver[11]. OCT has been extensively purified from rat liver[12] and found to be identical with the citrulline phosphorylase of KREBS et al.[13]. In mammals the enzyme is reported to occur almost exclusively in liver cells (REICHARD[14]). In accordance with this statement comparative studies of the OCT activity in different organs of the pig also revealed the opposite situation to that found in *Cottus quadricornis* L.; the transferase level in this case being more than 2000 times higher in the liver than that found in the pancreas[10].

GOT, GPT, and OCT activities expressed as units per 100 mg wet weight of pancreatic islet tissue, exocrine pancreatic parenchyma and liver tissue in *Cottus quadricornis* L. The figures represent mean values with their standard errors. The number of experiments are given within brackets.

	GOT	GPT	OCT
Islet tissue	206 ± 10 (6)	100 ± 4 (6)	132 ± 5 (6)
Exocrine tissue	206 ± 11 (6)	61 ± 4 (6)	133 ± 5 (6)
Liver	467 ± 22 (6)	80 ± 6 (6)	59 ± 5 (5)

Zusammenfassung. Im isolierten Inselgewebe aus dem Pankreas des Teleostiers *Cottus quadricornis* L. werden verhältnismässig hohe Aktivitäten von Glutaminoxalessigsäure-Transaminase (GOT), Glutaminpyruvatsäure-Transaminase (GPT) und Ornithin-Carbamyl-Transferase (OCT) gefunden)

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Antithyroid Activity of some 1-Alkyl Imidazolidine 2-Thiones

The antithyroid activity of some imidazolidine-5-thiones has recently been reported[1]. The screening of certain 1-alkyl imidazolidine-2-thiones for similar activity has been in progress in this Institute for sometime, and in view of the above report, we desire to record our observations, described below:

Materials and Methods. Male albino rats of the Institute Colony weighing 50 ± 4.2 g were challenged *subcutaneously* in groups of 8, each group with one of the compounds under test. Neomercazole (British Schering Ltd.) was used as an arbitrary standard of reference and was administered into one similar group, while another group was kept as control. Since some of the substances are insoluble in water, all were administered in 50% propylene glycol, which on previous test showed no untoward effect on the rat thyroid. The dose, which in each case was initially 1 mg/rat/day, was doubled from the 8th day and quadrupled from the 16th day, the volume of the injected fluid being kept throughout at 0.2 cm³/rat/day. The control animals received the menstrum alone. The last injection was given on the 21st day and the animals killed 24 h later. Both the thyroids were rapidly dissected out and weighed together. A few glands from each group were fixed in Bouin's fluid and processed for histological examination.

Results and Discussion. The data presented in the accompanying Table indicate that three of the compounds provoke increase in the weight of the thyroid of the animals under test, the order of activities being Isopropyl- > Ethyl- > propyl-compounds. The action of the butyl-

Mean thyroid weight of control (propylene-glycol-treated) and experimental animals, given 1-alkyl derivatives of imidazolidine 2-thiones

Group No.	Treatment	Mean thyroid weight[a] S.E. (mg)
1	Propylene-glycol (control) solution, 50%	16.5 ± 1.09 (8)[b]
2	1-ethyl imidazolidine 2-thione	11.6 ± 3.69 (8)
3	1-propyl derivative	27.6 ± 2.89 (8)
4	1-isopropyl derivative	51.6 ± 1.78 (8)
5	1-butyl derivative	13.2 ± 0.24 (8)
6	Neomercazole	13.6 ± 2.56 (8)

[a] Refers to the combined weight of both the thyroids.
[b] Number of animals treated.

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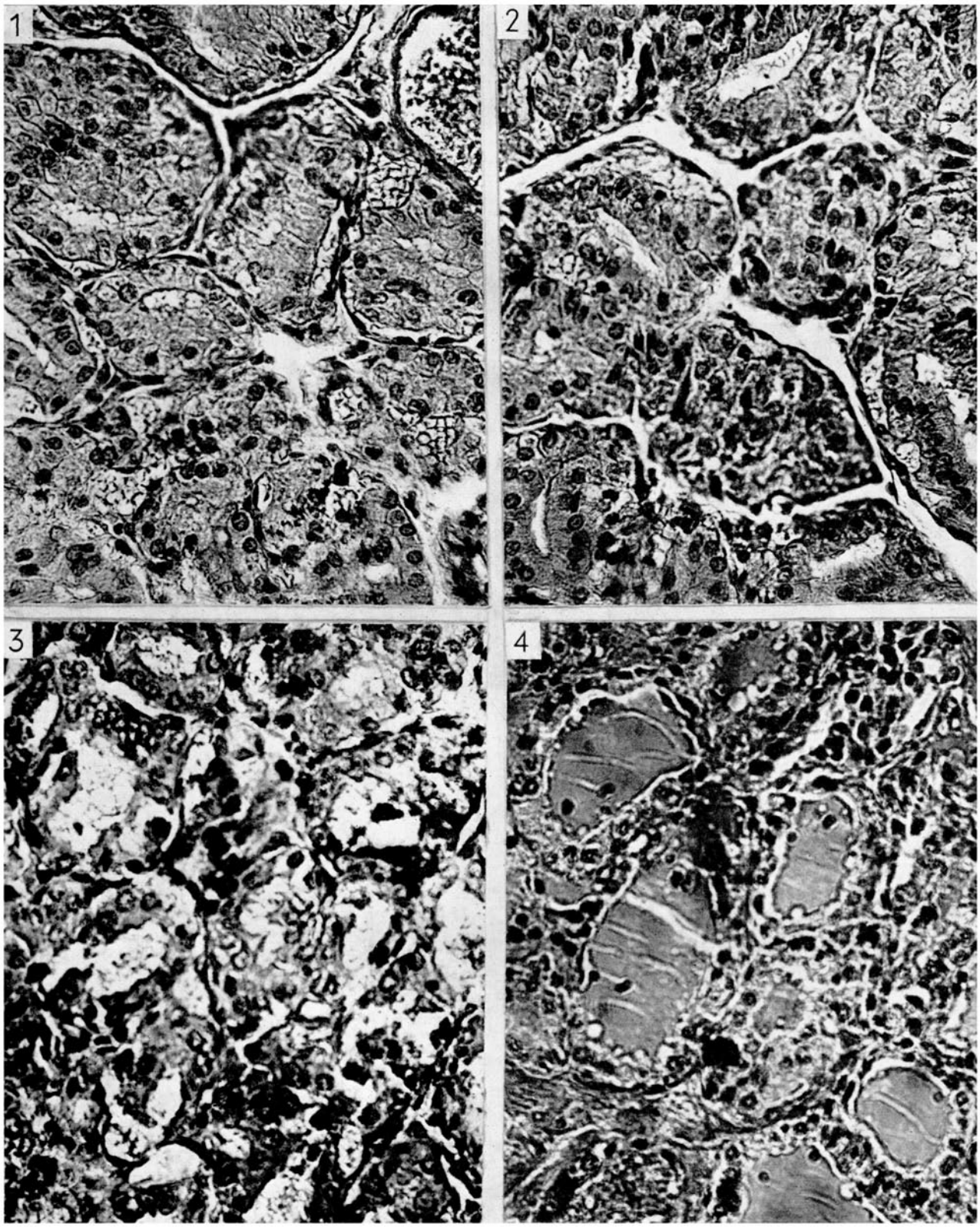

All sections 5μ thick, H & E stained, × 410

compound is rather inhibitory. The ethyl compound (I) appears to be at par with ($P = 0.44$) while the isopropyl compound (II) slightly superior to neomercazol, though such superiority is not statistically significant ($P = 0.16$).

Histological examinations of the thyroid glands of the animals treated with the active compounds reveal hypertrophy and hyperplasia of the acinar epithelium with little or no colloid in the lumen of the follicles. Figures 1 and 2 depict the thyroid pictures of animals treated with compounds I and II respectively. The corresponding pictures for neomercazole-treated and the control animals are presented in Figures 3 and 4 respectively.

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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Central Drug Research Institute, Lucknow (India), December 1, 1961.

[2] Our thanks are due do Drs. B. MUKERJI and M. L. DHAR for their keen interest in this work and to Dr. A. B. KAR for his helpful suggestion.

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].

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.

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

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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