Distribution of Antithyroid Activity in Tissues

CONTINUING our investigation of the antithyroid function of paraxanthine and related compounds1, we have carried out estimations of the antithyroid activity in mammalian tissues and blood.

All the extracts were made by methods similar to that described in our previous letter except that the purification was not carried beyond the mercury precipitate. The extracts at this stage contain other substances besides paraxanthine and it is possible that some of these are active. We have indeed evidence that suggests that the active substance in thyroid extracts is not identical with paraxanthine, though it appears to be related to it and may perhaps be formed from it in the body. Work on the identification of this substance is being continued.

In these circumstances we do not wish to contend that the active substance in any of the organs or fluids is paraxanthine, except that in liver, from which (as from urine1) paraxanthine has been isolated. It is, however, convenient to report the results in terms of paraxanthine, that is, as the concentrations of paraxanthine that would give the activities present in the extracts, and this we have done.

The true tissue contents will be higher than are given here owing to loss during the extraction. But since the process of extraction was similar for all the extracts, it is probable that the losses were of the same order in them all.

Antithyroid activity was estimated by the method described in the previous letter, in which use is made of the change of form of the temperature/heart-rate curve of the frog's heart. We have checked the accuracy of this method by estimating the paraxanthine in three solutions the strengths of which we did not know at the time of estimation. results were within 10 per cent of the true concentrations. We think that 20 per cent is the largest error that is likely to occur in the estimations. This error would not include losses during extraction.

Our results are given in the accompanying table. Each figure gives the result of extractions from a single sample of tissue, except the figures for liver which give the range of ten extractions.

Tissue	Source	Content
		μ gm. per gm. (wet weight)
Skeletal muscle	Cattle	1.2
Heart muscle	Cattle	2
Small intestine	Pig	1.7
Lung	Cattle	1.4
Liver	Cattle	0.2-0.9
Ovary	Cattle	8
Testis (immature)		4 5
Brain	Cattle	5
Spleen	Cattle	10
Thymus	Cattle	8
Pituitary	Cattle	8
Pancreas	Cattle	6
Thyroid	Cattle	500, 600, 750, 470.
Thyroid	Human (normal)*	600, 1,400, 750, 1,000, 833,
		666, 700, 800, 830, 850,
		770, 950.
Thyroid	Human (thyrotoxic)*	245, 133, 165, 105.
Thyroid	Human (adenoma)*	1,100, 1,100, 1,250.
Whole blood	Cattle	0.4 (per c.c.)
Whole blood	Pig	0.15 ,, ,,
Blood cells	Cattle**	0.0059 ,, ,,
Plasma	Cattle**	0.176 ,, ,,
* We are greatly indebted to Brof W M Turnbull of London		

*We are greatly indebted to Prof. H. M. Turnbull, of London Hospital, for these samples. ** From the same sample of blood. Content of the whole blood of this sample 0.132 μ gm. per c.c.

The most striking features of these results are: (1) the very high activity of the extracts of thyroid tissue on the average an extract of normal thyroid is 400-500 times as active as extracts of tissues such as muscle, intestine and lung; and (2) the wide variation of the activity of the thyroid extracts with the condition of the gland. In general, the concentration of antithyroid activity in the tissues runs parallel with the amount of iodine they contain. This is so in the thyroid as compared with other tissues, and it is also shown in the slightly higher contents of glandular tissues as compared with non-glandular². Our thyrotoxic thyroids came from patients which had been treated with iodine before extraction of the gland; they would have contained as much iodine as normal thyroids2. It is of interest to find that the antithyroid contents of thyrotoxic thyroids are relatively low even after treatment with iodine. G. S. CARTER.

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¹ Nature, 151, 728 (1943).

² Elmer, "Iodine Metabolism and Thyroid Function", 82, 86 (1938).

Anti-sulphanilamide Activity of 2-Aminopyrimidine-5-carboxylic Acid

THE observation of Woods1, that the anti-bacterial activity of sulphanilamide is inhibited by p-aminobenzoic acid, has been followed from time to time by observations recording a similar anti-sulphanilamide action for other compounds chemically unrelated to p-aminobenzoic acid. Thus Harris and Kohn² have shown that dl-methionine antagonizes sulphanilamide action. Martin and Fisher³ have reported that adenine possesses anti-sulphanilamide activity in mice infected with streptococci comparable with that possessed by p-aminobenzoic acid. Snell and Mitchell⁴ found that adenine, guanine, xanthine and hypoxanthine, as well as dl-methionine, reversed sulphanilamide bacteriostasis of certain lactic acid bacteria, although the results were largely dependent on the particular organism and conditions employed. Anti-sulphanilamide action has also been demonstrated with urethane5.

In the course of biological examination of some pyrimidines, we have recently examined 2-aminopyrimidine-5-carboxylic acide—an acid bearing a close structural relationship to p-aminobenzoic acid. It displayed no anti-bacterial action against Streptococcus pyogenes in vitro, but possessed distinct sulphanilamide inhibitory powers, although in smaller degree than p-aminobenzoic acid. Thus p-aminobenzoic acid was found to be 2,000 times as effective as 2-aminopyrimidine-5-carboxylic acid in inhibiting sulphanilamide bacteriostasis of Streptococcus pyogenes in vitro.

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