

c'est-à-dire une production rapide et importante d'anticorps isologues, facilement détectables par la méthode de précipitation en gélose, l'extrait tumoral chauffé ne provoque pas la formation d'anticorps précipitants mais induit cependant une réaction immunologique spécifique de type immunoallergique.

Une autre observation d'importance nous semble être la capacité de l'extrait tumoral chauffé à 100°C et contenant encore l'antigène, de reproduire fidèlement le syndrome foie-rate, l'accélération du pouvoir migratoire électrophorétique de l'albumine du sérum<sup>13,14</sup> et l'envahissement du foie par l'antigène tumoral spécifique<sup>15</sup>, phénomènes observés chez le rat porteur de la tumeur de Walker.

Nous voulons bien, d'autre part, attribuer l'ensemble des phénomènes non-spécifiques qui apparaissent à la suite de ces injections d'extraits tumoraux contenant ou non l'antigène spécifique aux toxines cancéreuses de NAKAHARA et FUKUOKA<sup>16</sup>. C'est ainsi que nous pensons que le catabolisme corporel, l'atrophie du thymus et l'hypertrophie des surrénales peuvent être dûs à la toxohormone de ces auteurs.

En ce qui concerne les changements sériques, il nous semble intéressant d'appuyer sur la dissociation entre les changements dans la distribution proportionnelle des protéines sériques qui sont indépendants de la présence de l'antigène tumoral dans l'extrait injecté et le changement du pouvoir migratoire de l'albumine qui n'est apparent que chez le rat recevant l'extrait qui contient encore l'antigène.

Des travaux antérieurs<sup>17,18</sup> ont d'ailleurs déjà démontré que les changements de concentration relative des différentes protéines du sérum ne sont pas exclusives au cancer ;

on les rencontre dans d'autres affections, notamment dans l'arthrite<sup>19</sup>.

**Summary.** When repeatedly injected to Fisher Inbred rats, boiled Walker tumour extracts induced non specific and specific reactions; non specific reactions being catabolism, thymus involution, adrenal hypertrophy and perturbation of serum proteins relative distribution. The specific reactions attributable to the presence of the specific tumoral antigen in the tumour extracts are immunoallergic arthritis, liver and spleen hypertrophy, acceleration of serum albumin electrophoretic migratory rate and the apparition of the specific antigen in the liver.

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<sup>13</sup> D. DUFOUR, L. BERLINGUET et J. M. LOISELLE, *Canad. J. Biochem. Physiol.* 37, 1401 (1959).

<sup>14</sup> D. DUFOUR et D. B. LINH, *Bull. Ass. franç. Et. Cancer* 48, 125 (1961).

<sup>15</sup> D. DUFOUR et D. B. LINH, *Bull. Ass. franç. Et. Cancer* 48, 3 (1961).

<sup>16</sup> W. NAKAHARA et F. FUKUOKA in *Advances in Cancer Research* Academic Press, New York 1958), p. 157.

<sup>17</sup> L. BONOMO *Reumatismo, Ital.* 9, 283 (1957).

<sup>18</sup> M. R. SHETLAR, C. CAHILL, G. STIDWORTHY et C. L. SHETLAR, *Proc. Soc. exp. Biol. Med.* 93, 44 (1956).

<sup>19</sup> Nous remercions Mme C.-G. PARÉ et M. J. PROULX pour leur collaboration.

## Transaminase and Transferase Activities in the Pancreatic Islet Tissue of the Teleost *Cottus quadricornis* L.

The rate of amino acid turnover into proteins is high in pancreatic tissue<sup>1</sup>. In making use of the fact that the islet tissue is concentrated into two macroscopically distinct bodies in the *Cottus* teleosts<sup>2,3</sup> it was possible to perform separate analyses of the *in vitro* formation of amino acids from glucose in the exocrine and endocrine parts of the organ<sup>4</sup>. Since the conversion of glucose into amino acids was particularly intensive in the islet tissue it was suggested that this would be an important metabolic feature of the islet cells in providing some of the amino acids necessary for hormone synthesis. The general importance of the transamination mechanism in the amino acid metabolism and the observation that glucose contributed in formation of comparatively high amounts of glutamic acid and glutamine prompted us to extend the analyses of the intermediary protein metabolism in the pancreatic islet tissue of *Cottus quadricornis* L. to the activities of glutamic-oxaloacetic transaminase (GOT) and glutamic-pyruvic transaminase (GPT). In addition the level of ornithine carbamyl transferase (OCT) was determined in the endocrine and exocrine parts of the pancreas and for comparative reasons also in the liver.

**Methods.** Adult bull's heads (*Cottus quadricornis* L.) of both sexes were kept for about 24 h in tanks with running fresh water. The animals were killed by decapitation and the tissue to be studied dissected out as rapidly as possible. The following samples were taken for analysis: the principal islets of the pancreas dissected free from capsular

tissue, the exocrine pancreatic tissue and liver slices. Because of the low weight of the endocrine pancreatic samples, tissues from 3 or 4 animals were pooled to give a total weight of about 30 mg. The samples were weighed and transferred to 1 ml ice cold 0.1 M phosphate buffer. After homogenisation the suspension was centrifuged and the supernatant removed and retained. The residue was resuspended in 1 ml phosphate buffer, centrifuged and this supernatant was added to the first. GOT and GPT were then determined as described by REITMAN and FRANKEL<sup>5</sup>. OCT was determined using the method of REICHARD<sup>6</sup>. In the latter case, however, the supernatant had to be diluted 5 times.

**Results.** The enzyme activities obtained in the three different tissue homogenates are presented in the Table as units per 100 mg wet weight. The value for GOT, similar in both the endocrine and exocrine parts of the pancreas (206), was less than half that obtained in liver (467). The level of GPT was highest in the islet tissue,  $100 \pm 4$ , and lowest in the acinar part,  $61 \pm 4$  ( $t = 6.80$ ;  $P < 0.001$ ). In comparing the GPT activities in the islet tissue and the liver the differences were probably significant ( $t = 2.65$ ;  $P < 0.05$ ). For OCT no difference was recorded between the endocrine,  $132 \pm 5$ , and exocrine,  $133 \pm 5$ , parts of

<sup>1</sup> E. HANSSON, *Acta physiol. scand.* 46, Suppl. 161 (1959).

<sup>2</sup> S. FALKMER, *Acta endocr. (Kbh.)* 37, Suppl. 59 (1961).

<sup>3</sup> S. FALKMER and B. HELLMAN, *Acta morph. neerl. scand.* 4, 145 (1961).

<sup>4</sup> B. HELLMAN and S. LARSSON, *Acta endocr. (Kbh.)* 38, 303 (1961).

<sup>5</sup> S. REITMAN and S. FRANKEL, *Amer. J. clin. Path.* 28, 56 (1957).

<sup>6</sup> H. REICHARD, *Scand. J. clin. lab. Invest.* 9, 311 (1957).

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

**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<sup>4</sup>. 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  $\alpha$ -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<sup>7-9</sup>. 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<sup>10</sup>.

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<sup>11</sup>. OCT has been extensively purified from rat liver<sup>12</sup> and found to be identical with the citrulline phosphorylase of KREBS et al.<sup>13</sup>. In mammals the enzyme is reported to occur almost exclusively in liver cells (REICHARD<sup>14</sup>). 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<sup>10</sup>.

### Antithyroid Activity of some 1-Alkyl Imidazolidine 2-Thiones

The antithyroid activity of some imidazolidine-5-thiones has recently been reported<sup>1</sup>. 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  $50 \pm 4.2$  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 cm<sup>3</sup>/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.

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 $\pm$ 10 (6)	100 $\pm$ 4 (6)	132 $\pm$ 5 (6)
Exocrine tissue	206 $\pm$ 11 (6)	61 $\pm$ 4 (6)	133 $\pm$ 5 (6)
Liver	467 $\pm$ 22 (6)	80 $\pm$ 6 (6)	59 $\pm$ 5 (5)

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

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<sup>8</sup> J. AWAPARA and B. SEALE, J. biol. Chem. **194**, 497 (1952).

<sup>9</sup> B. HELLMAN, S. LARSSON, and S. WESTMAN, Acta physiol. scand., **53**, 330 (1961).

<sup>10</sup> B. WRETLIND, K. ORSTADIUS, and P. LINDBERG, Zbl. Veterinärmed. **6**, 963 (1959).

<sup>11</sup> S. GRISOLIA and P. P. COHEN, J. biol. Chem. **191**, 189 (1951).

<sup>12</sup> P. REICHARD, Acta chim. scand. **11**, 523 (1957).

<sup>13</sup> H. A. KREBS, L. V. EGGLESTON, and V. A. KNIVETT, Biochem. J. **59**, 185 (1955).

<sup>14</sup> H. REICHARD, Scand. J. clin. lab. Invest. **9**, 103 (1957).

**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 <sup>a</sup> S.E. (mg)
1	Propylene-glycol (control) solution, 50%	16.5 $\pm$ 1.09 (8) <sup>b</sup>
2	1-ethyl imidazolidine 2-thione	11.6 $\pm$ 3.69 (8)
3	1-propyl derivative	27.6 $\pm$ 2.89 (8)
4	1-isopropyl derivative	51.6 $\pm$ 1.78 (8)
5	1-butyl derivative	13.2 $\pm$ 0.24 (8)
6	Neomercazole	13.6 $\pm$ 2.56 (8)

<sup>a</sup> Refers to the combined weight of both the thyroids.

<sup>b</sup> Number of animals treated.

<sup>1</sup> R. RINALDI and Y. BERNARD, Quoted from Chem. Abstr. **55**, 16787 g (1961).