STUDIES ON THE ACCUMULATION OF FLUOROBORATE IONS IN THE THYROID OF MICE

By

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ABSTRACT

The kinetics of accumulation of fluoroborate $^{18}\text{F}$ in the thyroid of mice were measured and compared with those of iodide. The kinetic behaviour of both ions was found to be identical. These findings corroborate former results on the analogy between the transport of fluoroborate and iodide ions into the thyroid gland.

Fluoroborate ions were shown to interfere with the accumulation of iodide in the thyroid gland (Anbar et al. 1959 a). Moreover, it was found that they accumulate in the thyroid to the same extent as iodide ions (Anbar et al. 1960). It has also been shown that the thyrotrophic hormone enhances the uptake of fluoroborate ions in analogy to its effect on iodide ions (Lewitus et al. 1962). The mechanism of accumulation of iodide ions in the thyroid and the effect of fluoroborate ions on this accumulation has recently been discussed (Halmi 1961).

The quantitative compatibility between iodide and fluoroborate ions in the transport mechanism of the thyroid, however, remained an open question (Halmi 1961). In order to elucidate this question, the kinetics of fluoroborate accumulation were carefully examined and compared with those of iodide. Reference is also made to previous results which corroborate the conclusions on the compatibility of $\text{BF}_4^-$ and iodide (Anbar 1963).

EXPERIMENTAL

$^{18}\text{F}$ labelled fluoroborate ions were prepared by isotopic exchange with fluoride $^{18}\text{F}$ ions, as has been described elsewhere (Anbar & Guttmann 1960; Askenasy et al. 1962). The specific activity of $\text{KB}^{18}\text{F}_4$ used in the present study ranged between 10–20 microcuries per mg.
0.1 ml of KB\textsuperscript{18}F\textsubscript{4} in neutral saline solution was injected into the posterior vena cava of albino mice (local strain, average weight 20 g). Laparotomy and injection were performed under light ether anaesthesia. At pre-determined time intervals, starting 30 seconds after the injection, the thyroid was cut off from circulation by cutting the arteries and veins, which had been exposed prior to the injection. Subsequently, the thyroid was excised together with a section of the trachea.

The accumulation of B\textsuperscript{18}F\textsubscript{4} in the thyroid was determined by measuring the total activity of the gland. As the radiochemical purity of the KB\textsuperscript{18}F\textsubscript{4} had been tested (Askensay et al. 1962), and the F\textsuperscript{−} activity did not exceed 0.5 %, little error was involved in counting the thyroid in the presence of the cartilage of the trachea. Another section of the trachea was, however, occasionally counted to determine the background due to the cartilage — this did not exceed 5 % of the total activity of the thyroid. The total activity was related to the dose injected, from which the percent injected dose present in the thyroid was calculated. The activity per gram of thyroid was calculated from the total activity, assuming an average of 4 mg for the thyroids of mice. This activity (counts per minute per gram tissue) was related to the activity of the blood (counts per minute per gram blood).

The kinetics of radioiodide accumulation in the thyroid were determined in a similar manner using Na\textsuperscript{131}I (carrier-free IBS 1, obtained from The Radiochemical Center, Amersham). A special procedure had to be adopted in order to follow the kinetics of accumulation of inorganic iodide without any interference of the organically bound iodine: After the thyroids had been counted, they were dialyzed for 1 hour against distilled water at a temperature of 4° C (Nagataki & Ingbar 1963) the water being changed several times. After all the inorganic iodide had thus been removed, the thyroids were re-counted, and the activity of inorganic iodide accumulated in the thyroid was calculated by subtraction. This procedure had to be undertaken in preference to the blocking of organic binding by propylthiouracil, as sulphhydryl-containing compounds were found to affect iodide transport (Halmi & Spirtos 1954).

**RESULTS AND DISCUSSION**

The kinetics of accumulation of BF\textsubscript{4} as compared with those of iodide ions are summarized in Table 1. It can be seen that the activity of B\textsuperscript{18}F\textsubscript{4} in the thyroid reaches a constant level within the first 60 seconds after the intravenous injection of the compound. Ten minutes after injection, the percent injected dose in the thyroid declined owing to the release of the fluoroborate into the circulation. It should be noted that the thyroid/serum ratio continues to increase, indicating that the kidney excretion of BF\textsubscript{4} is more rapid than its release from the gland. The activity of inorganic iodide in the glands follows a parallel pattern of behaviour. On the other hand, it is obvious that the activity of the organically bound iodine increases constantly within the first thirty minutes following injection. The difference between the absolute values of percent injected dose of BF\textsubscript{4} and I\textsuperscript{−} in the thyroids, is due to the difference in the specific activities of the two ions (cf. Anbar et al. 1959 b).

The complete parallelism between the kinetics of accumulation of fluoroborate and iodide ions supports the conclusion that these two ions are trans-
Table 1.

Kinetics of accumulation of $\text{B}^{18}\text{F}_4^-$ and of $\text{I}^{131}^-$ in the thyroids of mice.

<table>
<thead>
<tr>
<th>Time after i. v. injection (min)</th>
<th>$\text{B}^{18}\text{F}_4^-$ thyroid* injected dose (%)</th>
<th>$\text{I}^{131}^-$ whole thyroid injected dose (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>3.0</td>
<td>2.1</td>
</tr>
<tr>
<td>1</td>
<td>4.5</td>
<td>4.1</td>
</tr>
<tr>
<td>2</td>
<td>5.0</td>
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<tr>
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<td>6.0</td>
<td>5.5</td>
</tr>
<tr>
<td>10</td>
<td>8.5</td>
<td>6.0</td>
</tr>
<tr>
<td>30†</td>
<td>22.0</td>
<td>9.0</td>
</tr>
</tbody>
</table>

* counts per min per g tissue.
† Injected i. p.

reported into the thyroid by the same mechanism. In other words, the transport system seems unable to distinguish between these two ions. These findings eliminate the criticism raised by Halmi (Halmi 1961) about the presumably different rates of equilibration of iodide and fluoroborate.

Comparative quantitative experiments corroborate the analogy between the behaviour of fluoroborate and iodide ions (Anbar 1963). It has been found that the injection of 2 µmole of iodide into mice decreased the BF$_4^-$ accumulation in their thyroids by 20 ± 5% (from 20 T/S to 16). The same amount of ClO$_4^-$ decreased the T/S by 35 ± 5%, which is in complete agreement with previous findings on the action of BF$_4^-$ and ClO$_4^-$ on iodide uptake (Anbar et al. 1959 a). The complete analogy between the behaviour of fluoroborate and iodide ions has been further demonstrated by the finding that CNS$^-$ and F$^-$ inhibit BF$_4^-$ uptake in a manner similar to their action on iodide (i. e. a decrease of 45% in BF$_4^-$ uptake as compared with a 40% decrease in T/S of iodide, following the injection of 0.5 mg F$^-$ per mouse; a decrease of 50% in T/S of BF$_4^-$ as compared with a decrease of 60% of T/S of iodide, after the administration of 2 µmole NaCNS per mouse) (Anbar 1963). Furthermore, sulfhydryl-containing compounds were shown to have a similar action on BF$_4^-$ and iodide accumulation (Anbar 1963; Wollmann & Reed 1962). The transient
decrease in iodide uptake in animals treated with TSH (Halmi et al. 1960) is accompanied by a similar decrease in $\text{BF}_4^-$ accumulation (Anbar 1963). An increase of fluoroborate uptake with prolonged administration of TSH has also been demonstrated (Lewitus et al. 1962; Anbar 1963).

It may be concluded that the complete analogy between the physiological behaviour of iodide and fluoroborate ions at the transport stage in the thyroid has been satisfactorily demonstrated. From this result, however, it can not be deduced whether the accumulation of these ions in the thyroid is an active transport phenomenon or not.

In vitro studies carried out on thyroid slices (Wolff & Maurey 1963) have completely confirmed our previous conclusions that monovalent tetrahedral anions of an ionic size comparable to that of iodide are interchangeable with it in the transport system of the thyroid gland.

REFERENCES


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