JOURNAL OF NUCLEAR MEDICINE 7:287-289, 1966

In Vitro Effects of Different Rat Tissues on Radioiodinated Atabrine

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The *in vivo* distribution of radioiodinated Atabrine, proposed as a tagged material which can be selectively absorbed by some tumor tissues (1)(2), has been studied before (3). Because of the high amount of radioactivity found as radioiodide in the different tissues, we decided to perform an *in vitro* study of those tissues which showed the most radioiodide activity: liver, kidney, stomach and lung.

EXPERIMENTAL PROCEDURES

200 mg of the Wistar rat organs were finely minced and suspended in 2 ml of saline. Then 20 μC of ^{131}I labeled Atabrine, specific activity 0.12 mc/mg, dissolved in 1 ml of isotonic phosphate buffer solution pH 7.2 were added to the organ suspension and incubated at 37°C with occasional stirring, avoiding any evaporation. Radioiodinated Atabrine incubated under the same conditions but using saline solution instead of organ suspension was used as a blank.

After six hours of incubation 5 ml of methanol were added. The mixture was centrifuged at 2500 rpm after heating it five minutes and continuously stirring it in a waterbath at 50°C. Samples were taken of the supernatant and analyzed by ascending paper chromatography on Whatman paper 3 MM, using n-butanol saturated with 0.2 M phosphate buffer, pH 2.0, as a solvent. With this solvent the iodide Rf value is 0.16-0.19. The labeled Atabrine presents two compounds: one compound with Rf value 0.3-0.4, the same Rf as that for the unlabeled Atabrine, and another compound with Rf value 0.9-1.0. The chromatograms were scanned using a thin-window Geiger Müller tube with an automatic graphic recorder (Fig. 1, 2). The percentage of the total activity corresponding to each peak was determinated by integration.

RESULTS

In our experiment, performed in duplicate, all the organs showed a similar behavior. The fraction having Rf 0.9-1.0, compound B, disappears almost completely during the six hours and in the same time a corresponding amount of iodide appears. The fraction with Rf 0.3-0.4, compound A, decreases only by a very small amount (Table I). The highest decrease observed with liver is 19.0% of the activity initially present in this compound.

DISCUSSION

This *in vitro* deiodination of compound B is in accordance with the previous findings (1) of a high rate of radioiodide elimination after the administration of ^{131}I labeled Atabrine, containing 70% of compound B.

In experiments with other radioiodinated compounds such as 4-Iodo antipyrine, oleic acid and triolein performed in this laboratory, kidney, lung and stomach showed no such action *in vitro* after 15 hours of incubation. Contrary to these observations, in the case of radioiodinated Atabrine these tissues are capable of splitting the radioiodine tag from the labeled molecule to the same extent as the liver does (Table I).

Therefore, the biological system responsible for this deiodination seems to be other than the liver *nonspecific deiodinase* suggested by Chaikoff (4) and Straub (5) in the cases of thyroid hormone intermediates and radioiodinated 4-iodo antipyrine respectively.

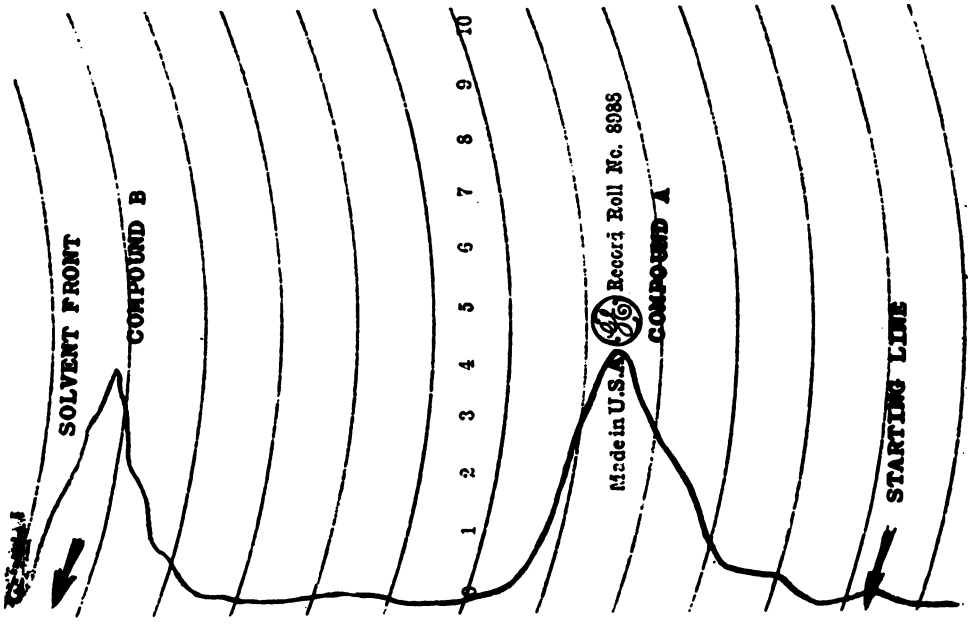

Fig. 1.- Radioactivity Scans of Chromatogram of the radioiodinated Atabrine, before incubation.

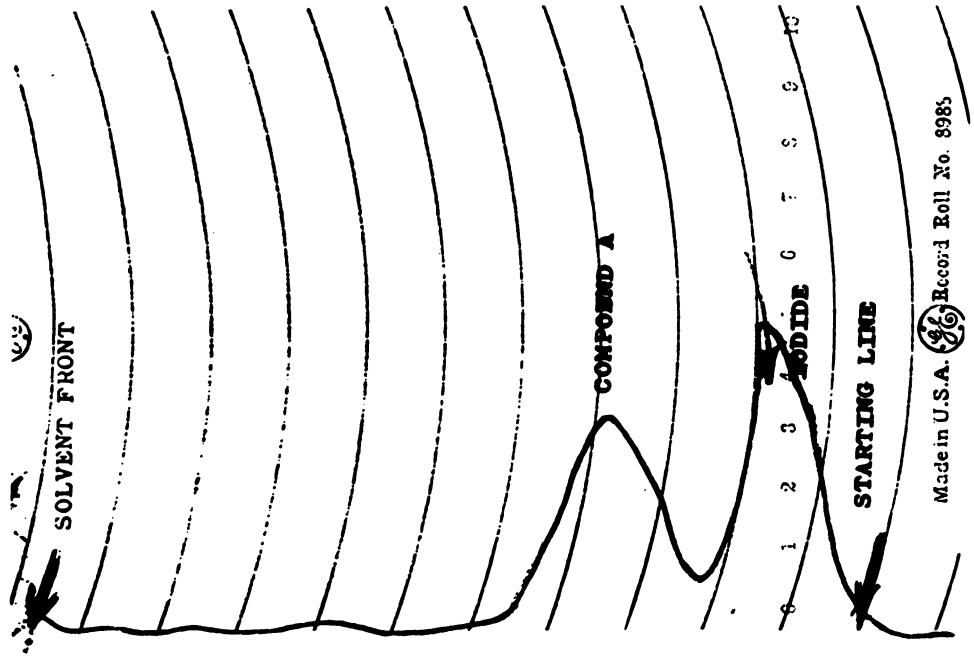

Fig. 2.- Radioactivity Scans of Chromatogram of the liver supernatant after 6 hours of incubation with radioiodinated Atabrine (Fig. 1).

TABLE I

Compound		*Stomach*	*Kidney*	*Liver*	*Lung*	*Blank*
A	1)	59.0	57.2	51.0	58.6	60.9
	2)	56.5	52.6	54.3	60.1	62.1
B	1)	2.0	1.5	0.6	0.0	37.8
	2)	3.6	3.2	0.4	0.6	35.7
Iodide	1)	39.0	41.3	48.4	41.4	1.3
	2)	39.9	44.2	45.3	39.3	2.2

Values of the radioactivity in the different fractions after six hours of incubation with various tissues, as percent of the total initial activity.

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