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3,507,618

APPARATUS AND METHOD FOR DETERMINING THYROID FUNCTION

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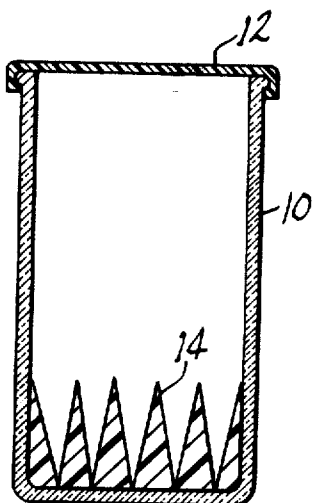


FIG-1

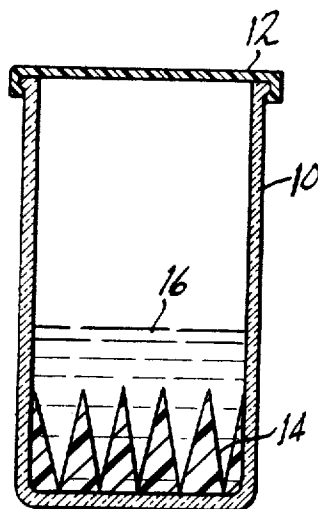


FIG-2

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3,507,618

APPARATUS AND METHOD FOR DETERMINING THYROID FUNCTION

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Int. Cl. G01n 31/04, 33/16

U.S. Cl. 23—230

14 Claims

ABSTRACT OF THE DISCLOSURE

Thyroid function determination comprising admixing a blood sample with a sheet having an anion exchanger and radioactive thyroxine or iodothyronine thereon, separating a portion of the treated sample and measuring its radioactivity, and apparatus therefor.

This invention relates to a new and improved apparatus and method for determining thyroid function.

Prior to this invention, various kits have been marketed for use in determining thyroid function by means of radioactive substances. One such type of kit entails a particulate resin having adsorbed thereon either radioactive triiodothyronine or thyroxine. In use, a sample of blood serum (or plasma) is thoroughly mixed with the resin, a portion of the blood sample is then separated from the resin, as by pipetting, and either the residual radioactivity of the resin or the radioactivity of the pipetted blood sample is measured. The ratio of this radioactivity to the radioactivity obtained using as a standard an equal portion of similarly treated blood sample drawn from a person having normal thyroid function determines whether the patient is hyperthyroid, euthyroid (normal) or hypothyroid.

The difficulty with this prior art process, however, resided in the use of a particulate resin. When a sample of blood was pipetted, a portion of the finely divided resin was often sucked up into the pipette along with the blood and the radioactivity of the triiodothyronine or thyroxine still adsorbed on such resin gave an abnormally high radioactive count to the sample.

It is an object of this invention, therefore, to provide a simple, improved apparatus for accurately determining thyroid function.

It is another object of this invention to provide a simple, improved method for accurately determining thyroid function.

These objects are achieved by the apparatus and method of this invention. It has been found that if an anion exchanger, such as an anion exchange resin, in sheet form and having adsorbed on the exchanger either radioactive triiodothyronine or thyroxine is used, the possibility of a portion of the exchanger being drawn into a pipetted blood sample is obviated, and truer, more meaningful determinations of thyroid function can be achieved.

The anion exchanger used can be any substance which will adsorb triiodothyronine or thyroxine, but preferably is an anion exchange resin, such as a polymer of styrene quaternary ammonium chloride, which is marketed by Rohm & Hass, under the trademark Amberlite IRA-400. The anion exchanger is bonded to a backing sheet, such as a strip of cloth or resin, such as polystyrene, as by the method disclosed in Reissue Patent 24,222, granted Sept. 18, 1956. Such anion exchange resin sheets are commercially available, the preferred sheet being one marketed by the Ionac Chemical Company under the trademark Ion Exchange Membrane.

To prepare the apparatus of this invention, the sheet of anion exchanger is first cut into pieces such as rectangles of about 3/4 inch by 1 1/2 inches. For ease of standardizing

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the tests, the pieces are preferably of uniform size. If an anion exchange resin sheet is used, such as the preferred sheet mentioned hereinbefore, it is preferably converted to its acetate cycle from the chloride cycle, the form in which it is sold, by washing with enough sodium acetate buffer pH 5.5 (0.2 M), either prior to cutting or prior to the next step.

The pieces are then placed in a container and a solution of radioactive triiodothyronine or thyroxine is added to the container. The preferred radioactive material is thyroxine-I¹²⁵, although thyroxine-I¹³¹, triiodothyronine-I¹²⁵ and triiodothyronine-I¹³¹ can also be used. The solution and sheet of anion exchanger are then thoroughly mixed to saturate the exchanger with the radioactive material. The pieces are then removed and dried and placed in the bottom of a container in which the test is to be carried out. Preferably the container is in the form of a test tube or vial of small enough diameter so that the sheet must be curled to be inserted into the container and is thereby frictionally retained in the container.

The test is preferably conducted in the presence of a buffering agent, such as one that buffers blood serum in the pH range of about 5 to about 5.5 (and optimally about 5.2 to about 5.3). Although any physiologically acceptable buffering agent may be used, the preferred buffers are sodium acetate (0.2 M, 5.5 pH), and trismaleate (0.2 M, pH 5.2). An aqueous solution of the buffering agent may be added to the blood sample prior to its contact with the anion exchanger or the buffer may be first added to the exchanger holding container, either just prior to use or previously. In the latter event, since the apparatus being marketed will be a container, such as a test tube or vial, containing the piece of exchanger sheet and a solution of the buffering agent, it must be capped to prevent spilling of the buffering solution.

In the accompanying drawings:

FIGURE 1 is a cross-section view of the device, in which the container 10 contains a piece of exchanger sheet 14, the container being closed with a cap 12.

FIGURE 2 is a vertical cross-section view similar to FIGURE 1 in which is included a blood serum solution 16.

In use, to one container (e.g., test tube or vial) containing the sheet of anion exchanger having adsorbed thereon the radioactive material (and also containing a buffering agent, if desired) is added a blood serum or plasma sample from the patient to be tested. Blood serum, rather than blood plasma, is preferable although either may be used. To a second container containing the same amount of initial radioactivity is added an equal volume of blood plasma or serum obtained from a person having normal thyroid function. Although the amount of these blood samples is not critical, for use in a five cc. vial, for example, about one ml. of plasma or serum is preferably used. The containers are then thoroughly agitated for sufficient time to assure complete removal from the anion exchanger of all radioactive material that can be removed by the blood sample being tested.

Equal volume portions of the thus treated blood sample from each of the containers are then removed and the radioactivities of these portions are counted. The ratio of the count of the radioactivity of the patient blood sample to the count of the radioactivity of the standard indicates the thyroid function. A low number, such as one less than 0.86, indicates hyperthyroid; a high number, such as one greater than about 1.20, indicates hypothyroid; and a reading in between indicates a normal thyroid function.

The following example illustrates the invention:

Polystyrene sheets having bonded thereto an anion exchange resin (MA 3148, Ionac Chemical Company equiv-

alent to Amberlite resin IRA-400, chloride cycle) are cut into pieces $\frac{3}{4}$ inch by $1\frac{1}{2}$ inches in size. These pieces are converted to the acetate cycle by mixing with acetate buffer (0.2 M, pH 5.5) several times. These are then washed with distilled water and placed in a container containing acetate buffer (pH 5.5). A solution of thyroxine- I^{125} in acetate buffer (pH 5.5) is added with stirring and the stirring continued for about one-half hour during which time most of the thyroxine is adsorbed on the resin. (The specific activity of the thyroxine solution should be such that 0.005 mgs. of thyroxine has a count of about 50,000.) The pieces are then washed with distilled water nad dried by pressing on a filter paper. They are then fluted and one piece each is placed in a 5 ml. vial. One cc. of patients' serum and 1 cc. of acetate buffer (pH 5.5) are added and the vial is shaken for 90 minutes. 1 cc. of the contents of the vial is then pipetted into a test tube and counted for I^{125} activity. A similar experiment is made using normal serum. The ratio of the counts in the patient's serum to that of the normal gives the diagnosis of thyroid function.

Similarly, by following the method of the example, but substituting thyroxin- I^{131} , triiodothyronine- I^{125} and triiodothyronine- I^{131} for the thyroxin- I^{125} , apparatus containing these respective radioactive agents, instead of thyroxin- I^{125} , are obtained.

The invention may be variously otherwise embodied within the scope of the appended claims.

What is claimed is:

1. A test for determining thyroid function which comprises intimately admixing a blood sample with a sheet having an anion exchanger and a compound selected from the group consisting of radioactive thyroxin and radioactive triiodothyronine thereon, separating at least a portion of the thus treated sample from the exchanger and comparing the radioactivity of the thus treated sample with a standard.

2. The test of claim 1 wherein the compound is radioactive thyroxin- I^{125} .

3. The test of claim 1 wherein the blood sample is blood serum and is admixed with the exchanger in the presence of a buffering agent which buffers the blood serum sample in the pH range of about 5.0 to about 5.5.

4. The test of claim 3 wherein the exchanger is an anion exchange resin.

5. An apparatus for determining thyroid function which comprises a container having therein a sheet having an anion exchanger and a compound selected from the group consisting of radioactive thyroxin and radioactive triiodothyronine thereon.

6. The apparatus of claim 5 wherein the compound is radioactive thyroxin.

7. The apparatus of claim 6 wherein the radioactive thyroxin is thyroxin- I^{125} .

8. The apparatus of claim 5 wherein the exchanger is an anion exchange resin.

9. An apparatus for determining thyroid function which comprises an elongated container closed at one end and opened at the other end and a sheet having an anion exchange resin and a compound selected from the group consisting of radioactive thyroxin and radioactive triiodothyronine thereon positioned in said container to be frictionally retained in said container when placed therein.

10. An apparatus for determining thyroid function which comprises a tube of circular cross section, closed at one end and opened at the other end, and a sheet having an anion exchange resin thereon of greater length than the diameter of said tube, said resin containing thereon a compound selected from the group consisting of radioactive thyroxin and radioactive triiodothyronine, whereby said sheet is positioned in said tube and frictionally retained therein.

11. The apparatus of claim 10 wherein the compound is radioactive thyroxin.

12. An apparatus for determining thyroid function which comprises a tube of circular cross section, permanently closed at one end and having a removable closure at the other end, and a sheet having an anion exchange resin thereon, said sheet being of greater length than the diameter of said tube and containing on the resin a compound selected from the group consisting of radioactive thyroxin and radioactive triiodothyronine, said sheet being positioned in said tube near the permanently closed end and frictionally retained therein.

13. The apparatus of claim 12 which also contains a solution of buffering agent that buffers in the pH range of about 5 to about 5.5.

14. The apparatus of claim 13 wherein the compound is radioactive thyroxin.

References Cited

UNITED STATES PATENTS

Re. 24,222 9/1956 Patnode et al. ----- 204—195

OTHER REFERENCES

K. Sterling and M. Tabachnick: J. Clin. Endocrin. 21, 456-464 (1961).

MORRIS O. WOLK, Primary Examiner

R. M. REESE, Assistant Examiner

U.S. Cl. X.R.

252—301.1; 260—2.1; 424—1, 2

UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

Patent No. 3,507,618

Dated April 21, 1970

Inventor(s) Dasika R. K. Murty, Klaus G. Florey

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 1, line 50, insert: "illustrated in the accompanying drawing" (to be inserted after: apparatus);

lines 58, 71, insert the number "14" (insertion after: anion exchanger);

line 72, "of" should be -- in;

Column 2, lines 37, 40, "cross-section" should be -- cross-sectional;

line 41, delete "blood serum", insert "buffering";

line 42, insert the number "10" after container;

line 45, insert the number "14" after anion exchanger;

line 48, insert the number "16" after blood serum;

Column 3, line 13, "nad" should be -- and;

Signed and sealed this 23rd day of July 1974.

(SEAL)

Attest:

McCOY M. GIBSON, JR.
Attesting Officer

C. MARSHALL DANN
Commissioner of Patents