# United States Patent [19]

Nouel

[11] 3,812,264

[45] May 21, 1974


[54] METHOD OF PRODUCING A CARRIER FOR A SCINTIGRAPHIC PREPARATION AND SCINTIGRAPHIC PREPARATIONS INCLUDING SAID CARRIER


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[22] Filed: **May 1, 1970**

[21] Appl. No.: **33,989**

[30] **Foreign Application Priority Data**

May 5, 1969 France ..... 6914129

[52] **U.S. Cl.** ..... **424/1,** 250/106 T, 252/301.1 R, 250/71.5 S, 424/131, 424/288

[51] **Int. Cl.** ..... **A61k 27/04**

[58] **Field of Search** ..... 424/1, 11, 101, 131, 288; 252/301.1 R; 23/230 B; 250/106 T, 71.5 S



[56] **References Cited**

OTHER PUBLICATIONS

Morcellet et al., Nuclear Sci. Abstracts, Vol. 24, No. 4, p. 617 No. 6078–Abstract from J. Biol. Med. Nucl: 4, No. 17, 16–18 (May–June 1969).

Journal de Biologie et de Midicine Nucleare A.T.E.N., Vol. IV, No. 15 pp. 20–24 (1969).



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[57] **ABSTRACT**

Scintigraphic carriers are obtained by sensitizing red blood corpuscles by means of a stannous chloride solution having a physiological pH. The carriers are then labelled with radio-active pertechnetate. The labelling efficiency is appreciably higher than in the known methods.


**5 Claims, No Drawings**

# METHOD OF PRODUCING A CARRIER FOR A SCINTIGRAPHIC PREPARATION AND SCINTIGRAPHIC PREPARATIONS INCLUDING SAID CARRIER

The invention relates to a method of producing a carrier for a scintigraphic preparation in which red blood corpuscles are sensitized by treatment with a stannous chloride solution. The invention also relates to a method of producing a scintigraphic preparation in which tin-sensitized red blood corpuscles are labelled with radioactive pertechnetate.

From Journal de Biologie et de Medicine Nucleaires A.T.E.N., vol. IV, no. 15, pages 20–24 (1969) it is known to produce a carrier for a scintigraphic preparation and to produce a scintigraphic preparation using this carrier by mixing blood with a 1 percent heparine solution and then centrifuging. The red blood corpuscles are subsequently suspensed in a medium consisting of a physiological salt solution, plasma gel and stannous chloride. The sensitized red blood corpuscles then are isolated according to known methods by centrifuging, after which they are brought into contact with radio-active pertechnetate. After a contact time of 30 minutes, they are again centrifuged and washed four times with a physiological salt solution. After resuspending in a physiological salt solution the preparation is ready for use. The labelling efficiency is 30 percent.

The invention provides a carrier by means of which scintigraphic preparations are obtainable in which the labelling efficiency is 90 percent. Obviously this is an important practical and economic improvement: the volume of the scintigraphic preparation to be administered to a patient can be reduced to one third; the losses of radio-active material have been reduced to one seventh.

The said improved efficiency is achieved by sensitizing the red blood corpuscles by means of a stannous chloride solution buffered to a physiological pH (about 7.4).

The invention thus relates to a method of producing a carrier for a scintigraphic preparation in which red blood corpuscles are sensitized by treatment with a stannous chloride solution characterized in that a stannous chloride solution is used that is buffered to a physiological pH.

The invention also relates to a method of producing a scintigraphic preparation in which red blood corpuscles are sensitized by means of a stannous chloride solution and then labelled with radio-active pertechnetate, which method is characterized in that for the sensitizing operation a stannous chloride solution buffered to a physiological pH is used.

As buffers any physiologically acceptable buffers may be used, such as alkali citrates, alkali tartrates, alkali phosphates, and the like.

Sensitization is effected by stirring a suspension of red blood corpuscles in a buffered stannous chloride solution for a short time, for example one or a few minutes. The excess of stannous ions is then removed. This may be performed by centrifuging the suspension and stirring the sediment in a washing liquid, which then is again centrifuged. The washing liquid may be a physiological salt solution. The excess of stannous ions may, however, be removed more effectively by adding a complex binder, for example ethylene diamine tetra-



acetic acid disodium salt (EDTA), either to the original suspension or to the washing liquid.

The amount of stannous chloride required for sensitization may vary within comparatively wide limits without appreciably influencing the labelling efficiency. As a rule, from 0.03 to 1.5 mg of $SnCl_2$ per 10 ml of blood is used.

Within a period of 9 days after the preparation of the carrier, the red blood corpuscles may be radio-actively labelled, for example by means of pertechnetate, without the labelling efficiency being affected. Labelling may be performed, for example, by a method as described in French Pat. 1,518,139.

The carrier may be packaged in bottles or injection syringes by conventional techniques. The radio-active labelling is preferably effected immediately prior to the use of the preparation.

The scintigraphic preparation can be used for blood tests, examination of the spleen, the heart, the brain, the blood vessels, and the like.

## EXAMPLE

a. 10 g of stannous chloride was dissolved in 1 ml of 10 N hydrochloric acid. The solution was added drop by drop to a solution of 2.715 g of trisodium citrate in 30 ml of distilled water. The volume was increased to 100 ml with distilled water, after which sodium hydroxide (about 3.5 ml) was added until the pH of the solution was 7.4.

1 ml of the resulting solution was added to 10 ml of venous blood. The mixture was stirred for 1 minute, after which 1 ml of a 5 percent ethylene diamine tetra-acetic acid disodium salt solution was added. After stirring again for 1 minute the liquid was centrifuged.

The sediment was taken up in 10 ml of a physiological salt solution, stirred and again sedimentated by centrifuging. Finally the sediment was again taken up in a physiological salt solution.

b. The preparation obtained by the method described in a) was radio-actively labelled with sodium pertechnetate by stirring it together with 1 ml of a pertechnetate solution taken from the radio-active milker for 20 minutes. The mixture was centrifuged and the sediment resuspended in 10 ml of a physiological salt solution, which treatment was repeated thrice.

The ready product has an activity of 700 $\mu$C.

It should be noted that the entire processing was effected under aseptic conditions.

What is claimed is:

**1.** A method of producing a carrier for a scintigraphic preparation, said method comprising subjecting red blood corpuscles to the action of a stannous chloride solution buffered to a physiological pH in an amount of, from 0.03 to 1.5 mg of stannous chloride per 10 ml of blood, and removing any excess of stannous ions.

**2.** A method of producing a scintigraphic preparation comprising subjecting red blood corpuscles to the action of a stannous chloride solution buffered to a physiological pH, in an amount of from 0.03 mg to 1.5 mg of stannous chloride per 100 ml of blood, removing any excess of stannous ions and then treating said red blood corpuscles with a pertechnetate thereby radioactively labelling said red corpuscles.

**3.** The method of claim **1** wherein trisodium citrate is used as a buffer.

**4.** A carrier for a scintigraphic preparation obtained by the method of claim **1**.

**5.** A scintigraphic preparation obtained by the method of claim **1**.

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PO-1050
(5/69)

# UNITED STATES PATENT OFFICE
# CERTIFICATE OF CORRECTION

Patent No. 3,812,264 Dated May 21, 1974

Inventor(s) JEAN-PAUL NOUEL

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

In the title page, Item [30], "6914129" should be -- 6914179 --.

Signed and sealed this 24th day of September 1974.

(SEAL)
Attest:

McCOY M. GIBSON JR.
Attesting Officer

C. MARSHALL DANN
Commissioner of Patents

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