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Recent Developments in Blood Cell Labeling Research

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ABSTRACT

A number of recent developments in research on blood cell labeling techniques are presented. The discussion relates to three specific areas: (i) a new in vitro method for red blood cell labeling with ^{99m}Tc; (ii) a method for labeling leukocytes and platelets with ^{99m}Tc; and (iii) the use of monoclonal antibody technique for platelet labeling. The advantages and the pitfalls of these techniques are examined in the light of available mechanistic information. Problems that remain to be resolved are reviewed. An assessment is made of the progress as well as prospects in blood cell labeling methodology including that using the monoclonal antibody approach.

INTRODUCTION

Radiolabeled blood cells have occupied an important role in diagnostic nuclear medicine procedures (6). Technetium-99m labeled RBC are routinely used for blood pool imaging, for the study of ventricular function and wall motion abnormalities of the heart, and for many other applications (25). The ^{111}In-oxine method of labeling leukocytes and platelets (6,35,36) is widely utilized in a number of clinical studies.

Most current labeling techniques are not ideal and need further improvement. As a result of research in cell labeling, newer and better techniques, suited for a more widespread use of labeled cells in research and clinical practice, have emerged. This article covers three specific areas: (i) a new *in vitro* technique for ^{99m}Tc-RBC labeling in whole blood; (ii) a kit method for labeling leukocytes and platelets with ^{99m}Tc; and (iii) the antibody approach of cell labeling, using as an example, the labeling of platelets with an antiplatelet monoclonal antibody. The existing methods are briefly described, followed by a discussion of the newer techniques and their advantages. Information on labeling mechanisms is presented where available, and problems that still remain are discussed.

RED BLOOD CELL LABELING WITH TECHNETIUM-99m

Labeling of RBC with ^{99m}Tc is routinely carried out using either *in vitro* or *in vivo* techniques (25,29). Methods developed over the past several years now provide high labeling yields with good label stability. Most procedures use Sn^{2+} (stannous) compounds for the *in situ* reduction of pertechnetate within the red cells since TcO_4^- does not bind effectively to the cells.

In vitro Methods

In *in vitro* methods, a small sample of blood is incubated with a stannous compound ("tinning" step), centrifuged to remove the plasma containing extracellular tin, and pertechnetate is added. To ensure good labeling, all extracellular tin must be removed quantitatively before adding pertechnetate, usually by washing the "tinned" cells with saline or, more effectively, with a solution of EDTA in saline (25,29). Kits containing lyophilized stannous tin complexed with a variety of ligands are usually employed. One such kit, a stannous citrate formulation, was developed at Brookhaven National Laboratory (BNL) in 1976 (23). A modified version of this kit (25,29) has been widely used during the past several years. The steps involved in this procedure are as follows: (i) Draw blood into Vacutainer kit tube; (ii) Incubate 5 min.; (iii) Add 1 ml 4.4% EDTA solution; (iv) Centrifuge; (v) Withdraw RBCs; (vi) Transfer to $^{99m}TcO_4^-$ vial; (vii) Incubate 5-10 min.; (viii) Assay and dilute for injection. The kit contains a freeze-dried mixture of stannous citrate (2 μg tin), 3.7 mg sodium citrate trihydrate, and 5.5 mg anhydrous dextrose. Labeling efficiences of >98% are routinely obtained.

In vivo Labeling

Labeling of RBC in vivo is carried out using the procedure initially described by Pavel and co-workers (21). Thirty minutes following the i.v. administration of stannous pyrophosphate (10-20 μg tin/kg body wt) into the patient, $^{99m}TcO_4^-$ in saline is injected. The RBC's are labeled immediately and the label has a clearance half-time in blood of about 50 ± 4 hr (2). The method is convenient and, therefore, widely utilized. A number of other tin complexes have been shown to work as effectively as tin pyrophosphate, but their superiority has not been established. Whereas in vitro methods consistently provide quantitative labeling of the cells, the in vivo labeling gives variable results (60-90%). This causes background problems in imaging and often makes quantification difficult. On the other hand, existing in vitro techniques are more cumbersome than the in vivo method since they require outside handling of the blood and involve undesirable centrifugation and washing steps.

The New Kit Method for In-vitro Labeling of RBC in Whole Blood

A new in vitro kit technique was recently developed (25) and refined to achieve simplicity and convenience comparable to the in vivo method. This method allows quantitative (>95%) and selective labeling of RBC using small (~1 ml) whole blood samples in a closed one-vessel operation. The kit consists of a stable, lyophilized mixture of stannous citrate (50 μg tin), 3.7 mg trisodium citrate, 5.5 mg dextrose, and <2 mg sodium chloride. The labeling protocol is as follows: (i) Draw 1 ml blood into heparinized syringe and add to the kit tube (or vial); (ii) Incubate 5 min with gentle mixing; (iii) Add 0.6 ml of 0.1% sodium hypochlorite solution, and mix; (iv) Add 1 ml 4.4% calcium disodium EDTA

solution or 1 ml ACD solution, and mix; (v) Add the desired quantity of ^{99m}Tc-pertechnetate in 0.5 - 3.0 ml saline; (vi) Incubate 15 min with gentle occasional mixing; (vii) Assay and dilute appropriately for injection; (viii) Incubate for 15 min at 49°C in place of step (vi) above, if a splenic agent (heat-damaged ^{99m}Tc-RBC) is desired.

This new "whole blood" method utilizes chemical inactivation (oxidation) of extracellular Sn^{2+}, and thus obviates the need for removing plasma by centrifugation and washing of the cells prior to the addition of pertechnetate. Since the cells stay in their native blood environment and since there is less handling and manipulation, technique-associated damage to the RBC is essentially eliminated. In addition, since no transfers are involved, aseptic conditions are easy to maintain. Finally, the uptake of tin by the RBC is much higher thereby eliminating the common drawback of other in vitro methods, namely, their limited reducing capacity for ^{99}Tc carrier.

Heart blood pool images in dogs and in man (29) demonstrate the effectiveness of this whole blood labeling method for ^{99m}Tc-RBC imaging applications, and clearly show the improved in vivo stability of the ^{99m}Tc label using this method. Briefly, in contrast to the previous methods, the release of ^{99m}Tc from the cells (producing $^{99m}TcO_4^-$) is considerably minimized and no thyroid or stomach uptake is seen with time. In a preliminary study in patients, the heart blood pool images were of high quality and good resolution (Fig. 1).

Mechanisms

Studies were undertaken to define the mechanisms involved in the in vitro (16,29) and the in vivo (25) methods for labeling RBC with ^{99m}Tc.

Factors such as (i) uptake kinetics and distribution of Sn^{2+} in blood components, using various stannous compounds, (ii) role of oxidation and chelation in the chemical inactivation of extracellular Sn^{2+}, (iii) uptake kinetics and distribution of ^{99m}Tc in "tinned" RBC, (iv) effect of carrier ^{99}Tc, (v) effect of plasma and other suspending media, (vi) sites of binding of Sn^{2+} and ^{99m}Tc within the RBC, and (vii) long-term retention of tin in RBC following in vivo labeling, were investigated. Representative results of these studies are summarized in Table 1 and Fig. 2.

Among the various ligands studied (32), citrate and glucoheptonate were most effective in transporting tin into the RBC (Fig. 2). The tin uptake depended on the total tin content of the kits, blood sample volume, ligand concentration, and temperature. The limiting factor (using 0.5 - 50 μg tin per ml blood) was not cell saturation. The uptake was rapid initially (5-10 min) and very slow thereafter. No uptake of stannic tin (Sn^{4+}) was seen. Removal of plasma tin before $^{99m}TcO_4^-$ addition (either by centrifugation or by adding NaOCl + EDTA or ACD to sequester and oxidize Sn^{2+} to Sn^{4+}) gave >95% ^{99m}Tc labeling of RBC. Using 50 μg kits + 1 ml blood, greater than 95% labeling yields were obtained with $^{99m}TcO_4^-$ solutions containing ^{99}Tc from up to 200 mCi of ^{99}Mo decay.

Association of ^{99m}Tc and tin with membrane and non-membrane (hemoglobin) fractions appears to be chemically similar; however, the binding of ^{99m}Tc to hemoglobin seems to have a greater ionic character than most metal-protein complexes. It is labile to dilution, to low ionic strength at neutral pH, and dissociates in an electrical field. In vivo

stability of ^{99m}Tc-RBC is attributable to the cell membrane that maintains a high hemoglobin concentration within the RBC and considerably slows the outward migration of reduced technetium species.

Blood clearance data in dogs showed that the EDTA treatment of tinned RBC conferred greater stability on the label. Compared to other in vitro methods, the blood clearance half-time was longest (35 hr) for ^{99m}Tc-RBC prepared using the new "whole blood" method.(29)

Evidence was found (cellulose acetate electrophoresis) for a small amount of plasma-bound Sn^{2+} species which resists oxidation by NaOCl. This species is slowly dissociable, however, and chelants such as EDTA or citrate (ACD) compete successfully for the plasma bound Sn^{2+} and render it oxidizable. Technetium-99m uptake by tinned RBC was adversely affected by low blood hematocrits (greater plasma content).

Following a single tin-pyrophosphate (Sn-PYP) injection in patients as in the in vivo labeling method, significant retention of Sn^{2+} was demonstrable even after a period of two months (2). Blood samples at up to 63 d after the Sn-PYP injection gave significant RBC labeling when incubated in vitro with ^{99m}Tc (Table 2).

The kinetics of labeling with the later blood samples were considerably slower indicating the incremental loss with time of Sn^{2+} from the RBC or its oxidation to Sn^{4+}. When pertechnetate was injected at various times following a single Sn-PYP injection, blood labeling was high at early time periods and decreased later (7 days, 41%; 42 days, 25%). The ratio of RBC to plasma activity of injected ^{99m}Tc also dropped significantly with time (7 days, 2.75; 42 days, 0.20) (25).

TECHNETIUM-99m LABELING OF LEUKOCYTES AND PLATELETS

While various investigators have attempted to label leukocytes and platelets with ^{99m}Tc, reported procedures provide neither sufficiently high labeling yields, nor satisfactory stability of the label. The described methods generally require large blood samples and utilize either the pretinning approach (12,25,32) or phagocytic mechanisms (in the case of polymorphonuclear leukocytes [PMNs]) (16), or lipophilic complexes (6,15,22,34). For pretinning the cells, a variety of Sn^{2+} complexes have been used, e.g., chloride, pyrophosphate, methylene diphosphonate, citrate, and others.(3,9,12,29,32) Both mixed white-cell populations and separated PMNs were used. Phagocytic labeling using ^{99m}Tc-colloids has been reported using a tin-technetium colloid (17), and ^{99m}Tc-sulfur colloid (7). The use of a ^{99m}Tc-HSA nanocolloid has also recently been reported (13,33).

We have carried out a detailed investigation in order to develop better kit methods for labeling lymphocytes, PMNs, and platelets with ^{99m}Tc (10,18,29,30,32). It was demonstrated earlier that among the various commonly used Sn^{2+} chelates, stannous-glucoheptonate (Sn-GH) is transported more effectively into cells and that the uptake appears nearly irreversible (25,29,32). Tin uptake by leukocytes was 11% (1.1 μg) from the 9.6 μg ^{113}Sn (GH) kit compared to only 1.7% (0.8 μg) from a 50 μg ^{113}Sn (citrate) kit. A similar trend is observed with platelets as well. Utilizing Sn-GH in a lyophilized kit, we obtained high labeling yields with ^{99m}Tc using the separated lymphocytes, neutrophils or platelets from as little as 4 ml of blood and only 10 μg of tin (Table 3 and Fig. 2). In vitro label stability was also high (~90%).

This general method was first reported in 1986 (10). Labeling yields are not affected significantly by cell concentration when 2-20 μg total Sn^{2+} is utilized in the procedure. The labeling protocol is as follows: (i) Reconstitute kit and add (10 μg Sn) to cells in saline; (ii) Incubate 15 min at 37°C and centrifuge 10 min at 400 g; (iii) Add 2 ml saline to cells; centrifuge 10 min at 400 g; (iv) Add $^{99m}TcO_4^-$ and incubate 15 min at 37°C; (v) Centrifuge and resuspend cells in autologous plasma for injection.

Studies were recently undertaken to better define the effect of the kit composition and the incubation and washing media on cell viability and function, and on labeling yields (18,30). Kits containing 10 or 100 μg tin with GH to tin ratios of 100 (kits A, B, and D) or 200 (kit C) to one were prepared and tested for labeling efficiency with separated lymphocytes and neutrophils. The pH was adjusted with NaOH from 5.5 (kits B, C, and D) to 7.8 (kit A), with free glucoheptonic acid available in kit D only. There was no statistical difference in labeling yields among the kits but kit D containing free glucoheptonic acid clearly damaged the cells. Kit C was used in <u>in vitro</u> tests of labeled neutrophils in the dog. The cell survival kinetics and distribution were markedly improved if PBS:saline (1:10) was used instead of saline for all wash steps, but the labeling efficiency was reduced by about 20%. The effect of tin and suspending media on platelet function and labeling was studied using aggregometry. <u>In vitro</u> viability for leukocytes was >90% (trypan blue exclusion), and satisfactory for platelets (~70% aggregability), when using the above procedure.

The advantages of the Sn-GH kit method are as follows: (i) Much less tin is needed to achieve a rapid and satisfactory intracellular Sn^{2+} content; (ii) Less Sn^{2+} remains extracellular, and thus, removal by oxidation or washing is easier and more effective; (iii) Highest ^{99m}Tc-labeling efficiences are obtained for RBC, leukocytes and platelets; (iv) Equally good labeling efficiencies are obtained with human, rat, rabbit, and dog cells; (v) Label stability in vitro is higher (2-3% washout from ^{99m}Tc-RBC, and ~10% from ^{99m}Tc-leukocytes and platelets, upon 24 hr incubation with saline or plasma); and (vi) Fewer cells are needed for labeling with clinically useful amounts of ^{99m}Tc (1 ml whole blood for RBC; leukocytes and platelets from ~4 ml blood). Fig. 3 shows a typical image in rabbits obtained with ^{99m}Tc-PMNs labeled using the Sn-GH kit procedure. At 2 hr after injection, intense localization of the activity was seen in the turpentine-induced abscess in the right leg, compared to the normal left leg area (Fig. 3B). The PMNs localized initially in the lungs and the liver and then cleared slowly from these organs and the blood (Fig. 3A). Kidney and bladder activity was high due to a significant, initial excretion of ^{99m}Tc.

Investigations are currently in progress to evaluate the in vivo effectiveness of leukocytes and platelets labeled with this method, in dogs. Detailed studies will be necessary to determine whether these labeled cells perform satisfactorily in the human system as well.

SPECIFIC CELL LABELING USING MONOCLONAL ANTIBODIES

Labeling of specific cell populations in whole blood samples would eliminate the possible damage from cell separation procedures and keep the cells in their native plasma environment throughout the labeling

procedure. Phagocytic labeling of PMNs with ^{99m}Tc colloids fulfills these criteria, although it is not clear whether the cells fully retain their chemotactic ability after being labeled using this procedure. A very promising approach is the labeling of cells with monoclonal antibodies directed against specific cell antigens. Various investigators have recently begun to actively search for cell-specific antibodies and have studied methods for *in vitro* and *in vivo* labeling of leukocytes (1,14) and platelets (8,19,20,24,26,27,29,37) in whole blood.

Our investigations on the use of an antiplatelet monoclonal antibody for specific platelet labeling (8,20,26,27,29) included developing suitable chemical methods to radiolabel the antibody with various nuclides including ^{123}I, ^{111}In, and ^{99m}Tc, investigating the binding of the labeled antibody with platelets in whole blood samples, and evaluating antibody-labeled platelets for imaging experimental thrombi and vascular lesions in dogs.

The antibody, 7E3, (IgG_1 subclass, directed against the fibrinogen receptor of the platelet surface) has been extensively studied and characterized during the last several years by Coller and co-workers (4,5). The antibody inhibits ADP-induced platelet aggregation, and the ADP-induced binding of fibrinogen to platelets. There are 50,000 antibody binding sites per human platelet, and 75,000 binding sites per dog platelet. The antibody cross reacts with dog platelets and was therefore chosen for further study.

In vitro studies with human and dog platelets showed that: there is only one type of binding site; greater than 90% tracer antibody dose binds to human platelets; ~70% of tracer dose binds to dog platelets;

there is negligible binding to other blood components; virtually all platelet-bound 7E3 becomes incorporated into thrombin produced clots; 10 μg antibody/ml blood causes total inhibition of platelet aggregation; and 0.5-1 μg antibody/ml blood did not produce any significant change in platelet function (4,5,27).

The antibody was iodinated by reacting 100 μg of 7E3 with radioiodide (^{123}I, ^{131}I) at a molar ratio of iodine to antibody of ~0.5, in the presence of 5 μg Chloramine T as the oxidant. The Iodogen technique was equally effective. TCA precipitation, polyacrylamide gel electrophoresis, and in vitro binding assay were used to characterize the product. Labeling yields (following purification) were 30-80% depending upon the reaction conditions, and the specific activity ranged between 20-300 μCi/μg (for ^{123}I at an average of <0.5 iodine atoms per antibody molecule). Labeling with ^{111}In was accomplished after conjugating DTPA to the antibody using the cyclic anhydride method (11). Labeling yields (using 100 μg antibody) were ~80% and the specific activity ranged between 10-40 μCi/μg at an average of 0.2 to 0.5 indium atoms per antibody molecule. Both iodine and indium labeled 7E3 displayed >90% binding specificity in the fibrinogen-coated bead assay.(20)

Blood clearance in dogs of the 7E3-labeled platelets showed that the initial recovery was ~70%, very similar to indium-oxine-labeled platelets. Approximately 50% of injected activity remained in the blood at 30 min, dropped to 40-45% at ~60 min, and then remained fairly constant up to 4 hr. Both iodine- and indium-7E3-labeled platelets showed a very similar blood clearance; plasma levels of indium were

~10% as opposed to ~5% for ^{123}I. Total urinary excretion at 4 hr was less than 2%.

Arterial and venous clots were produced in dogs either by thrombin injection into vein segments, by transcatheter placement of a copper coil into blood vessels, or by electrocoagulation. A 100-150 ml blood sample was incubated ex vivo with ~100 μg of ^{111}In-labeled 7E3 and the separated saline-resuspended cells were reinfused slowly into the animals. Three hr post-injection, clots in the lung were visualized despite the overlying heart blood pool activity. Clot-to-blood ratios in various imaging experiments ranged between 5 and 35. Fig. 4 shows the image in a dog with clots in the right common carotid artery, 90 minutes after injection of ^{111}In-7E3-platelets.

These studies have demonstrated that the antiplatelet monoclonal antibody, 7E3, binds with high selectivity to human or dog platelets in whole blood samples, and that the antibody could be labeled with ^{123}I and ^{111}In with high specific activity without loss of binding efficiency to platelets. In dogs, 7E3-labeled platelets generate early and clear images of experimental arterial and venous thrombi without the need for blood pool subtraction.

Thrombus localization using ^{131}I-7E3-platelets was compared with the ^{111}In-oxine-platelet technique in the same animals (8,26,27,29). The venous thrombi were clearly imaged within 5-30 min with ^{131}I-7E3-platelets and in ~60 min with ^{111}In-oxine-platelets. The clot to blood ratios were approximately twice as high as with ^{111}In-oxine-platelets. Coronary thrombi were visible ex vivo but only one-third of the time

in vivo at 3-4 hr after injection. Indium-111-oxine images at this time period were negative.

An advantage of the antibody technique over the conventional indium-oxine method is early imaging. In addition, cell separation is not required and a variety of nuclides can be employed, (e.g., ^{123}I, ^{99m}Tc, ^{97}Ru, etc.). Furthermore, an antibody chelate conjugate could be developed as a kit to make the procedure even more convenient. More rapid blood clearance of 7E3-platelets is, however, required to allow for prompt and reproducible imaging of coronary thrombi. This may become possible through a manipulation of the degree of substitution of the antibody on the platelets, or by using antibody fragments.

The clinical effectiveness of this procedure remains yet to be established, although preliminary experience of Peters et al. using a similar antibody (22) was encouraging.

CONCLUSIONS

Athough significant advances have been made in cell labeling research during the past ten years, the ultimate goal of labeling specific cell populations in whole blood with a variety of radionuclides tailored for particular applications has not been reached.

Monoclonal antibodies and their fragments, directed against specific cell surface receptors/antigens, appear particularly promising in meeting this challenge. Further research should lead to selective labeling of individual cell types. Some progress has already been made in the area of platelet and leukocyte labeling using the antibody approach.

In the meantime, several improvements in the currently available techniques are expected to provide better labeling yields, greater methodological convenience, and higher cell viability. Examples are the development of a new <u>in vitro</u> kit method for labeling red cells in small (~1 ml) whole blood samples with ^{99m}Tc, the tin-glucoheptonate method for labeling lymphocytes, polymorphonuclear leukocytes, and platelets with ^{99m}Tc, and the use of lipophilic ^{99m}Tc chelates for labeling leukocytes.

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FIGURE CAPTIONS

Figure 1 LAO projection in end diastole (left) and end systole (right) obtained in a patient following the administration of ^{99m}Tc-RBC prepared using the new BNL whole blood labeling procedure.

Figure 2 Technetium-99m labeling efficiencies (percent) for RBC, WBC, and platelets as a function of tin uptake using various tinning agents. Leukocytes and platelets were labeled at 37°C by incubating tinned cells, once washed, with $^{99m}TcO_4^-$ for 15 min. Red cells were labeled in 1 ml blood by the whole blood labeling method.

Figure 3 Images in a rabbit 2 hr following injection of ^{99m} Tc-labeled polymorphonuclear leukocytes. A, thorax and upper abdomen area; B, area of turpentine-induced abscess (arrow) in the right leg.

Figure 4 Anterior image of the neck area in a dog with experimental thrombi, 90 min following the injection of In-111-DTPA-7E3 labeled platelets. Clots in the right common carotid artery are visualized; there is no uptake in the normal left carotid area. The activity at the bottom of the picture is due to the heart blood pool.

TABLE 1 Tin and Technetium Distribution in RBC Following ^{99m}Tc-Labeling Using Stannous Citrate (^{113}Sn or ^{117m}Sn) Kits (n = 10)[a]

Tin (2+) Content of kit μg	RBC Bound Sn			RBC Bound ^{99m}Tc	
	Total Bound μg	% Membrane Associated	% Non-membrane Associated[b]	% Membrane Associated	% Non-membrane Associated[c]
2	0.43	4.0 ± 2.0	17.5 ± 9.6	1.7 ± 0.3	94.8 ± 2.0
5[d]	2.1	8.3 ± 1.3	34.2 ± 14.1	1.6 ± 0.4	84.5 ± 4.6
15	3.6	5.7 ± 2.9	18.3 ± 5.1	1.3 ± 0.4	93.3 ± 3.2
50[d]	5.25	0.5 ± 0.1	10.0 ± 5.1	21.8 ± 8.7	76.0 ± 8.9

[a] Whole blood method (using 1 ml) was used except for kits containing 2 μg tin.

[b] 90.1 ± 4.5% of non-membrane associated tin bound to heme; 12.9 ± 4.1% to globin.

[c] 18.3 ± 9.8% of non-membrane associated ^{99m}Tc bound to heme; 80.5 ± 10.0% to globin.

[d] n = 3

TABLE 2 *In vitro* RBC Labeling with ^{99m}Tc of Blood Samples Obtained at Various Intervals Following Sn-PYP Injection in Normal Human Volunteers (n = 4)

Time after Sn-PYP Injection	Percent Labeling Yield: Time (min) of incubation, RBCs + $^{99m}TcO_4^-$		
	15	60	300
30 min	98.5 ± 0.7	96.7 ± 1.2	--
24 hr	98.6 ± 0.3	98.4 ± 0.6	94.6 ± 2.3
7 d	55.7 ± 3.7	85.4 ± 5.8	96.5 ± 2.0
21 d	29.5 ± 4.3	47.6 ± 7.1	89.2 ± 5.2
42 d	21.4 ± 3.5	27.3 ± 6.8	61.7 ± 10.8
63 d	20.7 ± 13.7	31.7 ± 28.2	57.1 ± 30.1

TABLE 3 Technetium-99m Labeling Efficiencies (Percent) Using the Tin Glucoheptonate Kit Method

(n in parentheses)

Cells Used*	Human	Dog	Rabbit	Rat
Mixed WBC	74 ± 5 (21)	86 ± 2 (2)	-	76 ± 11 (3)
Lymphocytes	77 ± 5 (13)	87 ± 6 (2)	81 ± 5 (4)	-
PMNs	65 ± 10 (4)	77 ± 3 (2)	71 ± 5 (4)	87 (1)
Platelets	77 ± 5 (9)	96 (1)	78 ± 6 (2)	-

* From an average of 4 ml blood

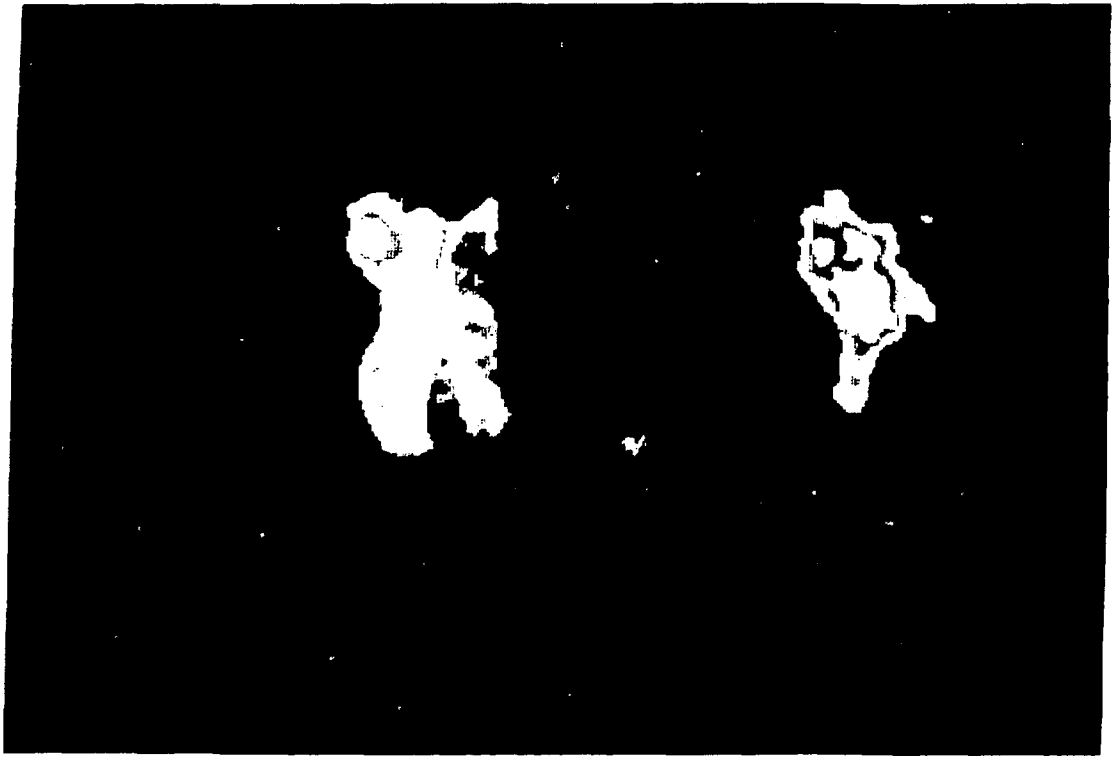
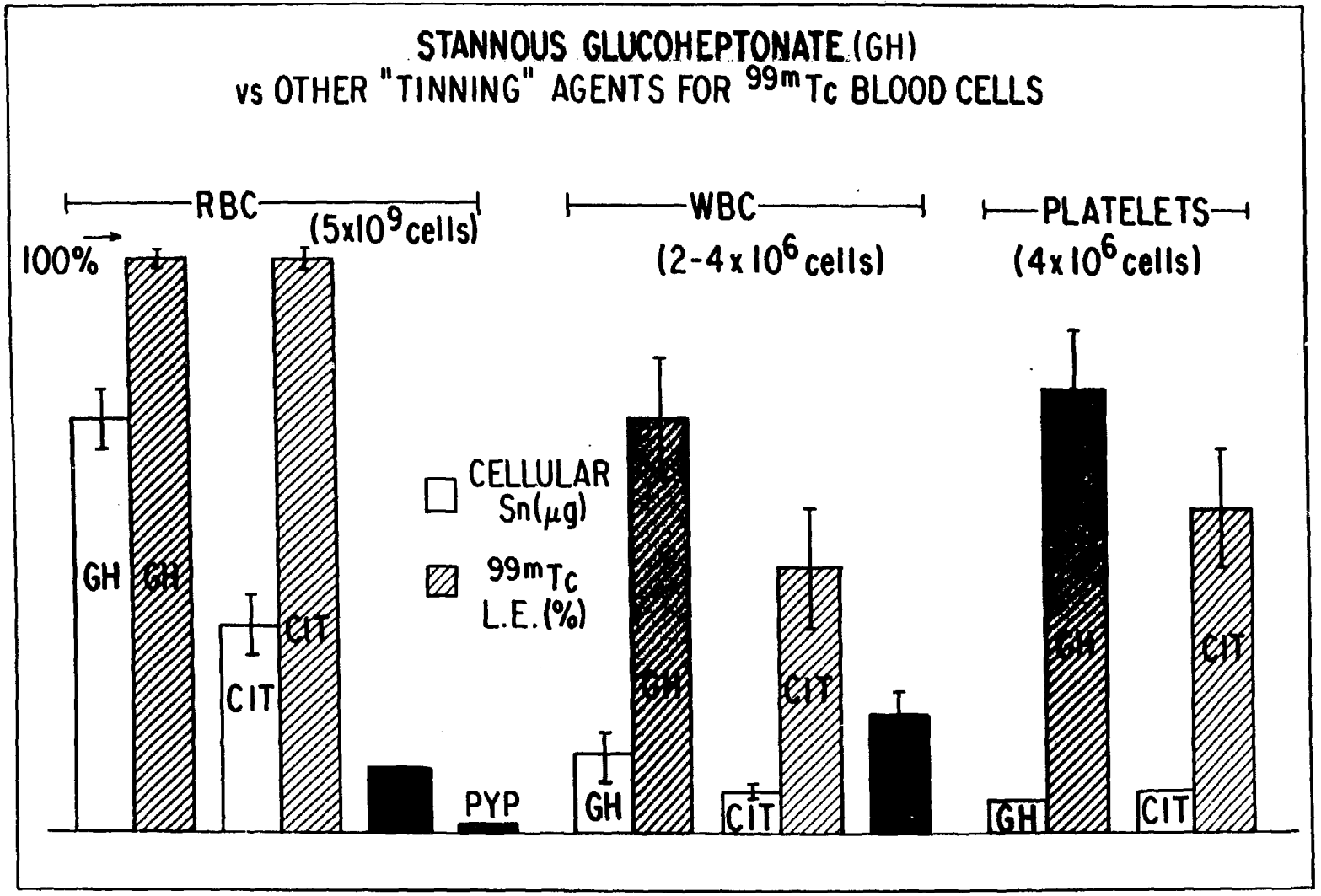


Fig. 1


STANNOUS GLUCOHEPTONATE (GH)
vs OTHER "TINNING" AGENTS FOR 99mTc BLOOD CELLS
RBC
(5x10^9 cells)
WBC
(2-4x10^6 cells)
PLATELETS
(4x10^6 cells)
100%
GH
GH
CIT
CIT
CELLULAR Sn(μg)
99mTc L.E.(%)
PYP
GH
GH
CIT
CIT
GH
CIT

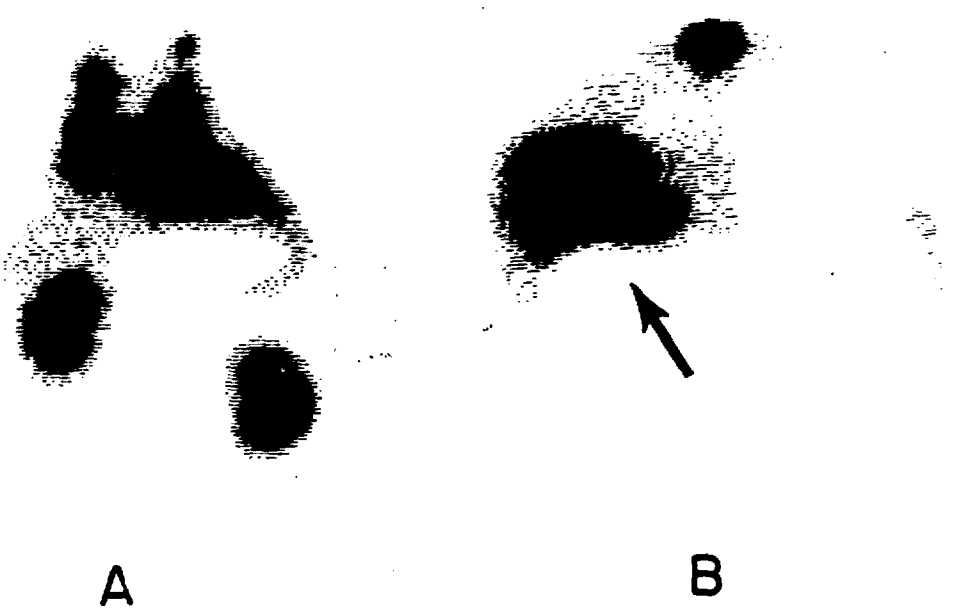


Fig. 3

Fig. 4