The effect of glucantime™ on the labeling of blood constituents with technetium-99m

Cecília Maria Carvalho Xavier Holanda[1], Rodrigo Carvalho Holanda Leite[2], Maria Teresa Jansem Catanho[3], Grace Maria Lima Souza[3], Mário Bernardo Filho[4].

Holanda CMCX, Leite RCH, Catanho MTJ, Souza GML, Bernardo Filho M. The effect of glucantime™ on the labeling of blood constituents with technetium-99m. Acta Cir Bras [serial on line] Available from: URL: htt://www.scielo.br/acb.

ABSTRACT – Purpose: The labeling of red blood cells (C) with ^{99m}Tc is employed in clinical nuclear medicine for a variety of diagnostic procedures. Drugs can alter this labeling method and modify the disposition of the radiopharmaceuticals. In this paper, the influence of glucantime on the labeling of blood constituents with ^{99m}Tc was reported. **Methods:** Blood was withdrawn from rats and incubated with glucantime. Stannous chloride and ^{99m}Tc were added. After centrifugation, plasma (P) and (C) were isolated. Samples of P and C were precipitated with TCA 5%, centrifuged and insoluble (IF) and soluble fractions (SF) separated. The percentages of total activity injected (%ATI) in C, IF-P and IF-C were calculated (p<0.05). **Results:** The %ATI on C decreased from control to following concentrations of glucantime (6.25%;12.5%;25%;50%;100%), respectively: 94.06±1.29 (control) to 77.15±2.79; to 76.68±1.88; to 75.15±2.79; to 72.64±4.40 and to 63.05±3.84. On IF-C the %ATI decreased from control to all the concentrations of glucantime (3.125%;6.25%;12.5%;25%;50%; 100%), respectively: 93.34±1.18 (control) to 78.81±2.76; to 74.76±4.82; to 74.02±5.32; to 64.35±4.82; to 62.81±1.97 and to 54.55±3.58. **Conclusions:** This effect was probably due to products present in this drug that may complex with ions (Sn^{+2} and $^{99m}TcO^{-}_{4}$) or have a direct or indirect effect on intracellular stannous ion concentration.

KEYWORDS: Glucantime™, Radionuclides, Sodium Pertechnetate, Technetium-99m, Stannous Chloride and Red Blood Cells.

Introduction

Antimonial compounds have formed the basis for the treatment of leishmaniasis since 1911. One of these antimonial compounds is N-methyl meglumine antimoniate, commercially known as Glucantime™ (Rhodia, Brazil), which is the preferred drug for the treatment of all clinical forms of leishmaniasis[1]. Human leishmaniasis is distributed worldwide, but mainly in the tropics and sub-tropics, with a prevalence of 12 million cases as well as an approximate incidence of 0.5 million cases of visceral leishmaniasis and 1.5 million cases of cutaneous leishmaniasis[2]. It is a parasitic disease caused by at least 17 species of the *Leishmania* protozoan parasite. The parasites are transmitted as flagellated promastigote forms from host to host by the bite of infected sandflies. In the mammalian host the parasites survive and multiply as an amastigote form in the phagolysosome of mononuclear phagocytes[3]. The antileishmanial activity of the glucantime™ occurs by interfering with glycolysis and b-oxidation of fatty acids in amastigotes, depleting intracellular ATP levels or by inhibiting the enzymes of the glycolytic via. This intracellular amastigote form, which survives and divides in tissue macrophages, thereby causing the disease, is the target for drug therapy (antimonial compounds, such as glucantime[3].

Another class of drugs that is used in human diseases, mainly for diagnostic procedures are the radiopharmaceuticals. In nuclear medicine, they represent a powerful tool in diagnostic and therapy procedures, as well as having contributed to the comprehension of many phenomena related to human beings[4].

The most widely employed radionuclide used as a radiopharmaceutical in nuclear medicine diagnostic procedures is technetium-99m (99mTc), in the form of sodium pertechnetate (Na99mTcO4). 99mTc has been used to label molecules, cells[4,5] biological species as *Dugesia tigrina*[6] and *Schistosoma mansoni*[7] and cellular structures such as leukocytes and red blood cells[8,9]. This radionuclide is the most frequently used in clinical nuclear medicine due to its wide availability from a 99-Molybdenum/Technetium-99m (99Mo/99mTc) generator, low radiation dose to the patient and low environmental impact[4,5].

The influence of drugs on the labeling of blood elements (red blood cells, plasma and cellular proteins) with ^{99m}Tc has been reported. Any drug that alters the labeling on the tracer could be expected to modify the disposition of the radiopharmaceuticals[4,5,10].

Red blood cells (C) labeled with 99mTc (99mTc-C) have come into wide use in clinical nuclear medicine for several important applications, including imaging of the cardiovascular system,

1.Universidade Federal do Rio Grande do Norte (UFRN), Centro de Biociências, Departamento de Microbiologia e Parasitologia. Av. Salgado Filho, nº 3000 - 59078-970, Natal/RN, Brazil.
2. Aluno do Curso Médico de Graduação-UFRN.
3.Prof. Dr. Da Universidade Federal de Pernambuco, Departamento de Biofísica e Radiobiologia e do Programa de Pós-Graduação em Ciências da Saúde-UFRN.
4.Prof. Dr. da Universidade do Estado do Rio de Janeiro, Instituto de Biologia Roberto Alcântara Gomes, Departamento de Biofísica e Biometria e do Programa de Pós-Graduação em Ciências da Saúde-UFRN.

detection and localization of gastrointestinal hemorrhage, measurement of red cell volume and spleen imaging. 99mTc-C may be done using an *in vitro* technique, by *in vivo* methods, or by a combination of these two, sometimes called *in vitro/ in vivo* labeling[11]. These labeling methods depend on the presence of a reducing agent, and stannous chloride is widely employed for this purpose[10,11].

The presence of medication (synthetic or natural drugs) in the patient's blood, as well as labeling conditions, can have an effect on the labeling of blood elements or can alter the characteristic and/or labeling process of the radiopharmaceuticals, changing their biological behavior and/ or labeling efficiency[5,10]. The procedures in nuclear medicine are based on the observations of a pattern of changes on the fixation of the radiopharmaceutical in specific targets. Unexpected alterations caused by factors other than disease may cause an imprecise diagnosis. Thus, the presence of the disease may be missed and/or underestimated[4,5,10].

There is no reported *in vitro* study of glucantime interaction with radionuclides. Therefore, in this study, we have evaluated the influence of glucantime on the labeling of red blood cells, plasma and cellular proteins with ^{99m}Tc using an *in vitro* procedure.

Methods

The experiments with the animals were carried out and the guidelines established by the Centro de Ciências da Saúde, Universidade Federal do Rio Grande do Norte were followed. The animals were not sacrificed in this work. Red blood cells were labeled with 99mTc using a previously reported procedure[6,7,8,9].

Heparinized whole blood was withdrawn from male *Wistar* rats (n= 9; 3 months old; 200-250g). Samples of 500mL of the blood were gently mixed and incubated with 100mL of different concentrations (3.125%; 6.25%; 12.5%; 25.0%; 50.0%; 100.0%) of glucantime solution, which were prepared using a saline solution (0.9% NaCl) as solvent. All these different concentrations were prepared using a solution pattern of glucantime (1,5g/5mL-Rhodia, Brazil), or with 100mL of 0.9% NaCl for the control samples, for 60 min, at room temperature. After this incubation period, a freshly prepared stannous chloride solution (500mL of 1.2 mg/mL), in the form of SnCl2.H2O (Reagen, Quimibrás Indústrias Químicas SA, Brazil), was added and the incubation continued for another 60 min. Then, 100mL of 99mTc (3.7MBq/mL), in the form of sodium pertechnetate, recently milked from a 99Mo/99mTc generator (Instituto de Pesquisas Energéticas e Nucleares, Comissão Nacional de Energia Nuclear, São Paulo, Brazil) was added and the incubation was continued for another 10 min. These samples were centrifuged (1500rpm/5min) and plasma (P) and red blood cells (C) were separated. Aliquots of 20mL of P and C were also precipitated with 1.0 mL of trichloroacetic acid (TCA) 5% and soluble fraction (SF) and insoluble fraction (IF) were isolated. The radioactivity in P, C, SF-P, IF-P, SF-C and IF-C was determined in a well counter (Clinigamma, gamma counter, LKB, Wallac, Finland). Thus, the percentage of radioactivity (%ATI) in each fraction was calculated, as previously described[6,7,8,9]. Briefly, to determine %ATI the radioactivity present in C, IF-P and IF-C was divided, respectively, by the radioactivity in P+C, IF-P+SF-P and IF-C+SF-C. The obtained values were multiplied by 100. The experiments were repeated nine times (different samples of whole blood withdrawn from three groups of 3 animals each) and the means and standard deviations were determined. Statistical analysis was performed by Kruskal-Wallis and Mann Whitney tests, $p<0.05$.

Results

Table 1 shows the distribution of radioactivity in C and P from blood treated with different concentrations of glucantime. Analysis of the results indicates that there was a significant ($p<0.05$) decrease in radioactivity uptake by C in the presence of glucantime from control (without glucantime) to the concentrations of glucantime (3.125%, 6.25%, 12.5%, 25%; 50% and 100%, respectively): from 94.06±1.29 (control) to 92.59±2.08; to 77.15±2.79; to 76.68±1.88; to 75.15±2.79; to 72.64±4.40 and to 63.05±3.84.

TABLE 1 – Effect of Glucantime™ on the labeling of Red Blood Cells (C) and Plasma (P) in the Blood with Technetium-99m (99mTc)

Concentrations of Glucantime (%)	(%ATI)	
	C	P
0.000(control)	94.06 ± 1.29	5.93 ± 1.29
3.125	92.59 ± 2.08	7.40 ± 2.08
6.250	77.15 ± 2.79	22.84 ± 2.79
12.500	76.68 ± 1.88	23.31 ± 1.88
25.000	75.15 ± 2.79	24.64 ±2.79
50.000	72.64 ± 4.40	27.35 ± 4.40
100.000	63.05 ± 3.84	36.94 ± 3.84

Samples of heparinized blood were incubated with glucantime™ solution (0.00%; 3.125%; 6.25%; 12.5%; 25.0%; 50.0% and 100.0%). Then, stannous chloride and 99mTc were added. These samples were centrifuged and plasma (P) and red blood cells (C) were separated. The %ATI in P and C was calculated. The values are the mean ± standard deviation. A statistical analysis (Kruskal-Wallis and Mann Whitney tests, $p<0.05$) was used to compare the results.

TABLE 2 – Effect of Glucantime™ on the labeling of Soluble Fraction (SF-C) and Insoluble Fraction (IF-C) of Red Blood Cells Proteins in the Blood with Technetium-99m (99mTc)

Concentrations of Glucantime (%)	(%ATI)	
	IF- C	SF- C
0.000(control)	93.34 ± 1.18	6.65 ± 1.18
3.125	78.81 ± 2.76	21.18 ± 2.76
6.250	74.76 ± 4.82	25.23 ± 4.82
12.500	74.02 ± 5.32	25.97 ± 5.32
25.000	64.35 ± 4.82	35.64 ± 4.82
50.000	62.81 ± 1.97	37.18 ± 1.97
100.000	54.55 ± 3.58	45.44 ± 3.58

Samples of heparinized blood were incubated with glucantime solution (0.00%; 3.125%; 6.25%; 12.5%; 25.0%; 50.0% and 100.0%). Then, stannous chloride and 99mTc were added. These samples were centrifuged and plasma (P) and red blood cells (C) were separated. Aliquots of C were precipitated with trichloroacetic acid (TCA) 5% and soluble fraction (SF) and insoluble fraction (IF) of C were separated. The %ATI in IF-C and SF-C was calculated. The values are the mean ± standard deviation. A statistical analysis (Kruskal-Wallis and Mann Whitney tests, $p<0.05$) was used to compare the results.

TABLE 3 – Effect of Glucantime™ on the labeling of Soluble Fraction (SF-P) and Insoluble Fraction (IF-P) of Plasma Proteins in the Blood with Technetium-99m (99mTc)

Concentrations of Glucantime (%)	(%ATI)	
	IF-P	SF-P
0.000 (control)	90.09 ± 2.72	9.90 ± 2.72
3.125	81.42 ± 5.81	18.57 ± 5.81
6.250	77.08 ± 4.28	22.91 ± 4.28
12.500	76.08 ± 3.18	23.91 ± 3.18
25.000	74.42 ± 5.51	25.57 ± 5.51
50.000	71.79 ± 5.01	28.20 ± 5.01
100.000	70.95 ± 3.16	29.04 ± 3.16

Samples of heparinized blood were incubated with glucantime solution (0.00%; 3.125%; 6.25%; 12.5%; 25.0%; 50.0% and 100.0%). Then, stannous chloride and 99mTc were added. These samples were centrifuged and plasma (P) and red blood cells (C) were separated. Aliquots of P were precipitated with trichloroacetic acid (TCA) 5% and soluble fraction (SF) and insoluble fraction (IF) of P were separated. The %ATI in IF-P and SF-P was calculated. The values are the mean ± standard deviation. A statistical analysis (Kruskal-Wallis and Mann Whitney tests, $p<0.05$) was used to compare the results.

Table 2 shows the distribution of radioactivity in soluble fraction (SF-C) and insoluble (IF-C) fraction of red blood cell proteins from blood treated with different concentrations of glucantime. Analysis of the results indicates that there was a significant ($p<0.05$) reduction in radioactivity fixation in IF-C from control to all the concentrations of glucantime (3.125%, 6.25%, 12.5%, 25%; 50% and 100%, respectively): 93.34±1.18 (control) to 78.81±2.76; to 74.76±4.82; to 74.02±5.32; to 64.35±4.82; to 62.81±1.97 and to 54.55±3.58.

Table 3 shows the distribution of radioactivity in soluble fraction (SF-P) and insoluble fraction (IF-P) of plasma proteins from blood treated with different concentrations of glucantime. Analysis of the results indicates that there was no significant (p>0.05) reduction in radioactivity fixation in IF-P with the tested glucantime concentrations when compared with control.

Discussion

The evidence that drugs can affect either radiolabeling or biodistribution of red blood cells in the context of nuclear medicine is indisputable. A number of researchers have turned their attention to *in vitro* testing of drugs with labeled red cells. A therapeutic drug can also modify the nature/amount of the ^{99m}Tc-radiopharmaceutical bound to blood elements and this may result in unexpected behavior of the radiopharmaceutica[4,5,9,10,11].

Any chemical, physical or biological agent which alters (i) the chemical identity of the tracer, (ii) the physiological status of the organ of interest, or (iii) its binding capability to plasma proteins or other blood elements, could be expected to modify the radiopharmacokinetic and disposition of the radiopharmaceutical in the specific target[4,5]. Some factors, such as red blood cells condition, excessive application of heparin, inadequate preparation of the reducing agent, (which is easily oxidized and must be prepared in a vacuum prior to its application), improper concentration of the reducing agent, poor quality of ^{99m}Tc and a number of devices, materials or agents interacting with the labeling elements/process can interfere in the labeling process[4,5,9,11].

When all these factors above were considered optimal, the presence of drugs and normal dietary intake in the blood stream may interact with blood elements or any component of the labeling process. In this case, they may: (i) act as an oxidant or a reducing agent; (ii) change the permeability of the cellular membrane or (iii) occupy the pertechnetate ($^{99m}TcO^-$) and/or stannous ions (Sn^{+2}) binding sites[4,9,11]. The oxidation effect would impair reduction of ^{99m}Tc by the stannous ion (stannous to stannic ion), compromising its binding and fixation of the radionuclide to the b-chain of hemoglobin. In contrast, the anti-oxidant effect would increase the red blood cell and plasma protein labeling efficiency, protecting the stannous ion from the oxidative process[4,5,11]. The cellular membrane permeability could impair the labeling process by compromising the active transport of the pertechnetate ion by blocking the anionic transport of band-3 protein, responsible for chloride/bicarbonate exchanges and possibly by the transport of the pertechnetate ion by blocking the calcium channels, impairing the stannous ion flow through the membrane[12], or causing morphological changes in the cellular membrane, hindering the free diffusion of the pertechnetate ion[4,5,11]. An *in vitro* method of labeling red blood cell and plasma proteins is a practical way of evaluating these effects.

In the labeling process of red blood cells with ^{99m}Tc, the stannous and pertchenetate ions pass through the plasma membrane. Sequential stages of the intracellular labeling process include reduction of 99mTc-pertechnetate by Sn^{2+}, subsequent binding of the reduced ^{99m}Tc to hemoglobin[5,10,12] and transmembrane transport of Sn^{2+} and $^{99m}TcO_4$ into the internal compartment of the red blood cells. The band-3 anion transport system and calcium channels may be involved in this transport[12].

We have previously shown that glucantime can alter the biodistribution *in vivo* of technetium-99m-methylenediphosphonic acid (^{99m}Tc-MDP) in *Wistar* rats[13]. Now, in this work, we have studied the effect of glucantime on the labeling of red blood cells, plasma and cellular proteins with ^{99m}Tc by *in vitro* process.

Glucantime is prepared by the reaction of pentavalent antimony with N-methyl-D-meglumine and the extent of polymerization in the composition of meglumine antimoniate may influence the pharmacokinetics of drug delivery, uptake by the reticuloendothelial system, and intracellular distribution of pentavalent antimony[14]. Although the exact mechanism of the effect of glucantime on the labeling of red blood cells is not fully made clear, we suggest that it may be explained (i) by a direct inhibition (chelating action) of the referred ions (Sn^{2+} and $^{99m}TcO_4^-$), (ii) by damage induced in the plasma membrane (membrane permeability), or (iii) by competition of the cited ions for the same binding sites (pertechnetate and stannous ions).

Red blood cell proteins can be labeled with ^{99m}Tc, mainly in the b-chain of the hemoglobin molecule[8,12]. The fixation of this radioactivity was likely modified by glucantime in all the concentrations. When these concentrations of glucantime were incubated with whole blood, there was a significant decrease in the fixation of ^{99m}Tc in the red blood cell proteins. This probably occurred due to the oxidation effect that would impair reduction of ^{99m}Tc by the stannous ion affecting binding and fixation of the radionuclide to the b-chain of the hemoglobin molecule[8,9,12].

Plasma proteins were also labeled with technetium-99m. ^{99m}Tc-labeled plasma proteins have been used to locate the placenta, to evaluate cardiac function and pulmonary perfusion, to determine blood volume and to study gastrointestinal protein loss[4,5,10]. The fixation of this radioactivity does not seem to be modified by glucantime solution. Another possibility is that there was a blocking of the labeling inside the cells, but the ^{99m}Tc (free) could be precipitated with the red blood cell ghost.

Studies performed evaluating the interference of *Maytenus ilicifolia*[15], *Paullinia cupana*[16] and other medicinal plants, revealed a reduction in C and P, indicating the presence of an oxidative effect, increasing the valence of stannous ion to +4 and reducing the fixation of the ^{99m}Tc.

In conclusion, our experimental data show that the labeling of red blood cell with technetium-99m and the fixation of this radionuclide to insoluble fractions of cellular proteins can be decreased in the presence of glucantime when an *in vitro* technique to label red blood cells is employed. We suggest that this effect may be due to the products present in this drug may (i) complex with these ions (Sn^{2+} and $^{99m}TcO_4^-$) or (ii) have a direct or indirect effect on intracellular stannous ion concentration. Furthermore, this study allows for the assessment of the effect of glucantime on direct or indirect oxidant properties.

References

1. Berman JD. Human leishmaniasis: clinical, diagnostic and chemotherapeutic developments in the last 10 years (review article). Clin Infect Dis 1997; 24:684-703.

2. WORLD HEALTH ORGANIZATION. World Health Organization. Division of Control of Tropical Diseases [on line] (http://www.who.int/tdr/diseases/leish/diseaseinfo.htm.). Accessed in November 10, 2003.

3. Balaña-Fouce R, Reguera RM, Cubria JC, Ordonez D. The pharmacology of leishmaniasis. Gen Pharmacol 1998; 30:435-43.

4. Thrall JH, Ziessman HA. Nuclear Medicine. 2ed. Boston: Mosby-Year; 2003. p 51-64.

5. Saha GB. Fundamentals of Nuclear Pharmacy. 4ed. New York: Springer-Verlag; 1998.p 131-140.

6. Bernardo-Filho M, Pires ET, Boasquevisque EM, Hasson-Voloch A. Studies on the incorporation of 99m-technetium to the platyhelminth *Dugesia tigrina*. Rev Parasitol 1993; 17: 7-11.

7. Bernardo-Filho M, Silva JRM, Reis RJM, Boasquevisque EM, Hasson-Voloch A. Conditions for labeling of *Schistosoma mansoni* cercaria with technetium-99m. J Nucl Biol Med 1992; 36:56-9.

8. Gutfilen B, Marinho JCA, Rozemblum S, Bernardo-Filho M. 99mTc-labeled leukocytes obtained with a suitable technique: the biodistribution study in rabbits. Acta Med Biol 1993; 41:193-6.

9. Braga ACS, Oliveira MBN, Feliciano GD, Reiniger IW, Oliveira JF, Silva CR, Bernardo-Filho M. The effect of drugs on the labeling of blood elements with technetium-99m. Curr Pharm Design 2000; 6:1179-91.

10. Hesslewood S, Leung E. Drug interactions with radiopharmaceuticals. Eur J Nucl Med 1994; 21: 348-56.

11. Kuehne R, Reuter E. High RBC labeling efficiency by controlling pretinning with the modified *in vivo, in vitro* labeling method. J Nucl Biol Med Technol 1999; 27: 222-6.

12. Callahan RJ, Rabito CA. Radiolabeling of erythrocytes with technetium-99m: role of band-3 protein in the transport of pertechnetate across the cell membrane. J Nucl Med 1990; 31: 2004-8.

13. Holanda CMCX, Jales RLC, Catanho MTJA, Leite RCH, Brito LML, Jales-Junior LH, Brandão KC, Amorim LF, Tiago GGB, Gomes ML, Bernardo-Filho M. Effects of the glucantime on the kinetic of biodistribution of radiopharmaceuticals in *Wistar* rats. Cell Mol Biol 2002; 48: 761-5.

14. Roberts WL, McMurray WJ, Rainey PM: Characterization of the antimonial antileishmanial agent meglumine antimonate (glucantime). Antim Agent Chemoth 1998; 42:1076-82.

15. Oliveira JF, Braga ACS, Avila AS, Caldeira-de-Araujo A, Cardoso VN, Bezerra RJAC, Bernardo-Filho M.. Assessment of the effect of *Maytenus ilicifolia* (espinheira santa) extract on the labeling of red blood cells and plasma proteins with technetium-99m. J Ethnopharm 2000; 72: 179-84.

16. Oliveira JF, Avila AS, Braga ACS, Oliveira MBN, Boasquevisque EM, Jales RL, Cardoso VN, Bernardo-Filho M. Effect of extract of medicinal plants on the labeling of blood elements with technetium-99m and on the morphology of red blood cells. I. A study with *Paullinia cupana*. Fitoterapia 2002; 73: 305-12.

Holanda CMCX, Leite RCH, Catanho MTJ, Souza GML, Bernardo Filho M. Efeito do glucantime™ na marcação de constituintes do sangue com tecnécio-99m. Acta Cir Bras [serial on line] Available from: URL: htt://www.scielo.br/acb.

RESUMO – Objetivo: A marcação de hemácias sangüíneas (C) com ^{99m}Tc é muito utilizada nos procedimentos diagnósticos na medicina nuclear. Drogas podem alterar este método de marcação e modificar a biodisponibilidade de radiofármacos. Neste trabalho, foi avaliada a influência de glucantime na marcação de elementos sangüíneos com ^{99m}Tc. **Métodos**: Sangue foi retirado de ratos e incubado com glucantime. Adicionou-se cloreto estanoso e ^{99m}Tc. Após centrifugação, plasma (P) e (C) foram isolados. Amostras de P e C foram precipitadas com TCA 5%, centrifugadas e separadas em frações solúveis (FS) e insolúveis (FI). Os percentuais de atividade total injetada (%ATI) em C, FI-P e FI-C foram calculados ($p<0,05$). **Resultados**: O %ATI em C diminuiu, em relação ao controle, nas seguintes concentrações de glucantime (6,25%;12,5%;25%;50%;100%), respectivamente: 94,06±1,29 (controle) para 77,15±2,79; para 76,68±1,88; para 75,15±2,79; para 72,64±4,40 e para 63,05±3,84. Em FI-C, o %ATI diminuiu, em relação ao controle, em todas as concentrações de glucantime (3,125%;6,25%;12,5%;25%;50%; 100%), respectivamente: 93,34±1,18 (controle) para 78,81±2,76; para 74,76±4,82; para 74,02±5,32; para 64,35±4,82; para 62,81±1,97 e para 54,55±3,58. **Conclusões**: Este efeito provavelmente foi devido a produtos presentes nesta droga que podem se complexar com íons (Sn^{+2} e $^{99m}TcO_4^-$) ou ter um efeito direto ou indireto na concentração intracelular do íon estanoso**.**

DESCRITORES: Glucantime. Radionuclídeos. Pertecnetato de sódio. Tecnécio 99m. Cloreto estanoso. Hemácias.

Corresponding author:
Dra Cecília Maria de Carvalho Xavier Holanda
Universidade Federal do Rio Grande do Norte (UFRN)
Departamento de Microbiologia e Parasitologia
Centro de Biociências
Av. Senador Salgado Filho, 3000
59078-970 – Natal, RN - Brazil
E-mail address: cechol@ufrnet.br (Cecília M. C. X. Holanda)
Fax number: +55-84-211-9210
Phone: +55-84-215-3437
Supported by: Universidade Federal do Rio Grande do Norte, Universidade Federal do Rio de Janeiro, Universidade Federal de Pernambuco and Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ) - Brazil