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PREPARATION AND CONTROL OF ^{68}Ga RADIOPHARMACEUTICALS

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Preparation and Control of ^{68}Ga Radiopharmaceuticals

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ABSTRACT

Development of the ^{68}Ge-^{68}Ga generator and its applications in nuclear medicine are reviewed. The preparation of radiopharmaceuticals labeled with ^{68}Ga is described. Clinical and animal studies with ^{68}Ga as ^{68}Ga-EDTA for brain tumor localization, ^{68}Ga-citrate for uptake in bone, and ^{68}Ga-ferric oxide colloid for bone marrow scanning are presented. The preparation of ^{68}Ga-polymetaphosphate-Mg-polymetaphosphate for kidney scanning and ^{68}Ga-chromic phosphate for liver scanning is described. The radiation dose and toxicity of these radiopharmaceuticals are given.

Procedures are suggested for maintaining and testing the sterility and apyrogenicity of ^{68}Ga elutions from the generator.

The future usefulness of ^{68}Ga for scanning in nuclear medicine is evaluated on the basis of improved radiopharmaceuticals and greater availability of instrumentation for imaging with positron emitters.

INTRODUCTION

The rapid advances in instrumentation available for diagnostic scintigraphy, which allows studies to be completed in a short time, increase the importance of developing radiopharmaceuticals labeled with short-lived radionuclides. Since most clinical studies using scintillation cameras or scanners are not done near a direct production site for radioisotopes, it becomes increasingly important to obtain the maximum benefits from radioisotope generators, which provide a convenient and economical source of short-lived radionuclides.

An ideal generator should have a long half-life parent isotope strongly adsorbed on ion-exchange material from which the short-half-life daughter can be rapidly eluted in high radiopurity with a physiologically suitable eluant solution. The ^{68}Ge-Ga generator meets, to a high degree, these requirements of an ideal generator system.

Germanium-68, $T_{1/2}$ 275d, decays 100% by electron capture to ^{68}Ga, $T_{1/2}$ 68 min, which decays 88% by B$^+$ emission and 12% by electron capture to stable Zn. The principal gamma-ray emission of ^{68}Ga is the 511-keV positron annihilation gamma emission with less than 4% higher-energy gamma emissions [1]. Gallium-68 is one of the few useful positron-emitting isotopes that can be obtained from a generator system, because most B$^+$ emitting nuclides, being neutron deficient, are produced by cyclotron irradiation.

Gallium-68, as a generator-produced isotope, offers the following advantages: (a) ^{68}Ga has a short half-life, which reduces radiation exposure to the patient and permits rapid buildup to equilibrium amounts in the generator from which the ^{68}Ga activity can be eluted every 3 to 4 hours; (b) the high yield of B$^+$ emissions make it useful for coincidence detection systems such as the positron scintillation camera; (c) the long half-life of the parent, ^{68}Ge, extends the useful life of the generator and reduces the cost of ^{68}Ga; and (d) ^{68}Ga can be used to label useful radiopharmaceuticals.

GENERATOR DEVELOPMENT

The development of the ^{68}Ga generator derives from the work of Gleason, who developed a "positron cow" which used solvent extraction with acetylacetone to separate ^{68}Ga from ^{68}Ge [2]. Subsequently, Greene and Tucker developed an improved ^{68}Ga generator which used column chromatography with alumina (Al_2O_3) as the adsorbent for ^{68}Ge [3]. This versatile, yet simple, separation procedure provides a generator system that is easy and reliable to operate while yielding a ^{68}Ga product of high radiopurity (less than 10^{-3}% ^{68}Ge contamination) even over extended milkings with 25 liters of 0.005 $\underline{M}$ EDTA (ethylene-diaminetetraacetic acid). A method for obtaining ^{68}Ga, as a sterile and isotonic solution for medical use, has been reported [4]. Sterility of the product solution is accomplished by passing the ^{68}Ga-EDTA eluate through a sterile 0.22-μ Millipore filter retained in a Swinnex hypodermic adaptor. Sterile and pyrogen-free reagents and glassware are used for the elution of ^{68}Ga with 10 ml of 0.005 $\underline{M}$ EDTA at pH 7.8. Saline solution (0.5 ml of 18%) is added for isotonicity, and the ^{68}Ga activity is assayed either by a calibrated ionization chamber (Mediac) for direct readout of activity in mCi or by counting the 511-keV annihilation gamma emissions in a well counter with pulse-height selection and using a calibrated standard of ^{22}Na or ^{68}Ge. This preparation of ^{68}Ga-EDTA is a useful brain-scanning agent.

BRAIN SCANNING

^{68}Ga-EDTA has been used with coincidence detection systems to visualize brain lesions. Anger and Gottschalk used ^{68}Ga and the positron scintillation camera to study patients with brain tumors [5]. Shealy et al.

have studied the uptake of ^{68}Ga in intracranial lesions [6]. It is known that ^{68}Ga-EDTA is normally excluded by the blood-brain barrier, but that it will be taken up in tumors in which the permeability is increased.

A comparison of brain scanning using ^{68}Ga-EDTA and the positron scintillation camera with ^{203}Hg-neohydrin and the focused collimator scanner was reported by Gottschalk et al. [7]. They reported, in the twenty patients studied, that ^{68}Ga-EDTA was as successful as ^{203}Hg in detecting brain tumors. For a 700- to 750-μCi dose of ^{68}Ga injected intravenously, the radiation dose was calculated to be <30 mrads whole body and <150 mrads renal. ^{68}Ga positron camera pictures were obtained in 4 to 10 min. ^{68}Ga reduces the radiation and shortens the examination time in brain scans, but it is not so tumor-specific as ^{203}Hg-neohydrin. Less vascular (slow growing) gliomas are not visualized with either ^{68}Ga-EDTA or ^{203}Hg-neohydrin.

Schaer et al. [8] reported on the diagnosis of 96 case studies with ^{68}Ga-EDTA and the positron camera for detection of brain lesions. In these studies, 50 cases were classified as abnormal. Of these, 41 were confirmed as abnormal and nine were false positives. Of the remaining 46 cases classified as negative, five were false negatives.

^{68}Ga CHEMISTRY

For the preparation of other ^{68}Ga radiopharmaceuticals which require a chemical reaction with ionic Ga^{+3}, it is necessary to free ^{68}Ga from the EDTA chelating agent. This can be accomplished by at least three different methods. The first method involves extracting carrier-free ^{68}Ga into diisopropyl ether from the EDTA eluate which has been made 7.5 $\underline{N}$ in hydrochloric acid, and then back-extracting the ionic ^{68}Ga into H$_2$O [9]. The second method uses mg amounts of carrier gallium to free the ^{68}Ga from EDTA by exchange with ionic Ga [10]. In the preparation of ^{68}Ga-citrate for a 70-kg patient, using a total of 140 mg of carrier Ga (2 mg/kg), there are 5% ^{68}Ga-EDTA and 95% ^{68}Ga-citrate when the eluant solution is 20 ml of 0.005 $\underline{M}$ EDTA. The exchange reaction must be done in 0.5 $\underline{N}$ HCl, with heating to insure rapid exchange between ^{68}Ga and carrier Ga [10]. The third method produces ^{68}Ga-citrate by evaporating the ^{68}Ga-EDTA eluate to dryness in a platinum crucible under a heat lamp, ashing the residue at about 400°C for 20 min, and dissolving the ash in 2% (W/V) citric acid [11].

BONE SCANNING

Hayes et al. [9,10] have used ^{68}Ga citrate for bone scanning by utilizing the effect of carrier gallium on the distribution of ^{68}Ga. Table I shows the effect of carrier gallium on the 2-hr distribution of ^{68}Ga-citrate in the rat. In going from carrier-free to high levels of gallium (10 mg/kg), the uptake in bone increased by a factor of 2 while the percentage uptake in other tissues, except for the kidneys, decreased. In the presence of 5 mg Ga per kg body weight and a molar ratio of citrate to gallium of 3:1, there was rapid uptake of ^{68}Ga-citrate in the bone (30% injected dose).

In studying 36 patients with ^{68}Ga-citrate, Hayes [10] found that bone lesions were detected by scanning before they were roentgenographically visible. The estimated radiation dose is 400 mrads/mCi to the bone and 76 mrads/mCi to the whole body.

Edwards [12,13] and Ahumada et al. [14] used ^{68}Ga-citrate in skeletal scans of patients with known or suspected bone lesions. In 56 skeletal scans on 46 patients, they found 13 patients with positive scans that corresponded to known or demonstrated skeletal lesions. Positive scans were found not only in metastatic lesions, but also in fracture, myelofibrosis with osteosclerosis, and inflammatory or degenerative arthritis. Metastatic bone lesions were demonstrated when the radiopharmaceutical contained 2 to 4 mg of stable gallium per kg of body weight. Because of the toxicity of gallium [LD_{10} 20 mg per kg body weight (15)], this procedure is limited to its application for bone scanning in patients.

Recent investigations by Weber et al. [11] as shown in Table II indicate that ^{68}Ga compares favorably in photon yield and radiation dose with ^{18}F and [87m]Sr for bone scanning. However, the ratio of bone to soft tissue is lower for ^{68}Ga, even in the presence of up to 10 mg Ga per kg (rat).

BONE MARROW SCANNING

Gallium-68, as hydrous ferric oxide colloid, has been used for bone marrow scanning by Hayes et al. [16,17]. The colloid is prepared by hydrolysis of ferric chloride in the presence of ionic ^{68}Ga, which is completely bound by the colloid. Localization is rapid in the liver, spleen, and bone marrow. Concentration ratios are bone marrow to bone, 100; bone marrow to blood, 200; and bone marrow to liver, 1.5. Based on animal uptake studies, the estimated radiation dose in a human subject is 1.6 rad/mCi to bone marrow, 0.75 rad/mCi to liver, and 1.5 rad/mCi to spleen. One mg Fe per kg body weight together with 90 mg dextran per kg body weight enhanced the uptake of [68]Ga (1.32% inj. dose/g) in the bone marrow of rabbits 1 hour after administration of the isotope, as shown in the data from Table III.

Knisely et al. [18] found that ^{68}Ga ferric oxide colloid compares favorably with ^{99m}Tc sulfur colloid for obtaining bone marrow scans in two patients with leukemia. Blood clearance studies with ^{68}Ga ferric oxide colloid gave a half-time of 2 min, with about 1% remaining in the blood at 30 min. This compares with a clearance half-time of 7 min for technetium sulfur colloid, with about 10% of the injected dose remaining in the blood 30 minutes after intravenous administration of the isotope.

The toxicity of ferric oxide colloid was studied by Nelson et al. [19]. Doses up to 10 mg Fe per kg (10 times the dose proposed for human use) were injected into rabbits and dogs. No reactions to the aggregates were noted and no significant histological abnormalities were detected in lungs, adrenals, or kidneys.

KIDNEY SCANNING

Anghileri [20] has described a new compound, ^{68}Ga-polymetaphosphate-Mg-polymetaphosphate, for kidney scanning. The material is prepared by evaporating the ^{68}Ga-EDTA eluate to a small volume, adding 1 ml of 0.1 $\underline{M}$ $MgCl_2$ as the carrier, and coprecipitating ^{68}Ga with $Mg(OH)_2$ by adding concentrated NH_4OH. Freshly prepared polymetaphosphoric acid is added until the precipitate of $Mg(OH)_2$-^{68}Ga dissolves at pH 3 to 4. The pH of the solution is adjusted to 7 with $NaHCO_3$ solution. The radiopharmaceutical is sterilized by Millipore filtration. Tissue distribution, as per cent of the injected dose in rats, 1 hr after intravenous injection, is 40% in kidneys, 3.1% in liver, and 1.9%/ml blood. The radiation dose to the kidneys is about 10 rads/mCi. No toxic symptoms were noted during the experiment.

LIVER SCANNING

Anghileri and Prpic [21] have reported on a colloidal ^{68}Ga compound, ^{68}Ga-chromic phosphate, for liver scanning. The first part of the method is similar to that for making the kidney scanning agent: coprecipitation of ^{68}Ga is done with $Mg(OH)_2$, which is dissolved with HCl acid solution. The pH is adjusted to neutral and this solution is added to 0.3 ml of CrO_3 (10 mg/ml), 0.3 ml of H_3PO_4 (10 mg/ml), and 1 mg Ga^{+3} as $GaCl_3$. The mixture is heated at 90-100ºC and 10 to 15 mg of Na_2SO_3 in 2 ml of 3% gelatin is added; 0.2 ml of $NaHCO_3$ is added, and heating is continued for 5 min. The final solution is sterilized by autoclaving. Tissue distribution of the administered dose in rats 15 min after intravenous injection is 90.6% in liver, 3.9% in spleen, and 0.86%/ml of blood.

STERILITY AND PYROGEN TESTING

Edwards and Hayes [22] present some suggestions for controlling sterility and nonpyrogenicity of radiopharmaceuticals obtained from long-lived generators. Because of the short half-life of ^{68}Ga, quality control testing is not feasible. However, periodic elution samples are tested by standard U.S.P. methods for sterility and pyrogenicity to confirm the integrity of the procedure. Furthermore, aliquot samples are taken from each preparation for testing if pyrogen contamination is suspected because of a febrile reaction in the patient. All the reagents and apparatus used for the preparation of short-lived radiopharmaceuticals are sterile and pyrogen-free. Aseptic techniques are used throughout the procedure, and the generator is stored in a sterile glove box. The long half-life of the parent, [68]Ge, prolongs the useful life of the generator over a period of 6 to 12 months, which increases the chances of contamination.

[68]Ga generators are commercially available (NENC), and can be ordered with a Luer fitting on the column for the attachment of sterile Millipore filters retained in Swinnex adaptors. The ^{68}Ga-EDTA eluate can be collected directly into an evacuated sterile vial. The yield of ^{68}Ga from the generator with 10 ml of 0.005 $\underline{M}$ EDTA (based upon the [68]Ge activity) is 30% 1 hour after a previous elution, 55% after 2 hours, and 70% after 4 hours. The [68]Ge leakage is less than 0.01% for each elution.

By using sterile and pyrogen-free ^{68}Ga generators that are eluted through a closed system, the chances of contaminating the generator with each elution are minimized.

CONCLUSIONS

Gallium-68 can become more useful for scanning when improved radiopharmaceuticals and coincidence detection systems become more readily available. Radiopharmaceuticals can be improved by using different chelating agents such as DTPA (diethylenetriaminepentacetic acid) for a better tumor-to-brain ratio of 30:1, compared with the 20:1 for EDTA. For bone scanning, less toxic carrier elements than gallium might prove useful for saturating the blood protein binding sites and improving the uptake in bone [23].

Charkes [24] classified ^{68}Ga as possessing 13 of 14 requisites of a good bone scanning agent. By this rating ^{68}Ga compares favorably with ^{18}F and ^{87m}Sr. The major disadvantage of ^{68}Ga-citrate for bone studies (besides the need for toxic carrier gallium) is the lower uptake ratio of bone to soft tissue.

Radiopharmaceuticals might be developed for uptake in other organs. Colombetti [25] has proposed ^{68}Ga-labeled macroaggregates for lung studies. Many of the radiopharmaceuticals labeled with ^{113m}In can probably be labeled with ^{68}Ga, because these two elements are closely related in their chemistry. Since ^{68}Ga is a positron emitter, superior resolution could be gained by utilizing the coincident gamma emissions of positron annihilation. Anger [26] has developed a positron scintillation camera with tomographic capabilities which will be useful in determining the depth of localization and could make B$^+$-emitting nuclides increasingly important for clinical scanning.

REFERENCES

[1] LEDERER, C.M., HOLLANDER, J.M., PERLMAN, I., Table of Isotopes, Wiley, New York (1967).

[2] GLEASON, G.I., A positron cow, Intern. J. Appl. Radiation Isotopes 3 (1960) 90.

[3] GREENE, M.W., TUCKER, W.D., An improved gallium-68 cow, Intern. J. Appl. Radiation Isotopes 12 (1961) 62.

[4] YANO, Y., ANGER, H.O., A gallium-68 positron cow for medical use, J. Nucl. Med. 5 (1964) 485.

[5] ANGER, H.O., GOTTSCHALK, A., Localization of brain tumors with the positron scintillation camera, J. Nucl. Med. 5 (1964) 326.

[6] SHEALY, C.N., ARNOW, S., BROWNELL, G.L., ^{68}Ga as a scanning agent for intracranial lesions, J. Nucl. Med. 5 (1964) 161.

[7] GOTTSCHALK, A., McCORMACK, K.R., ADAMS, J.E., ANGER, H.O., A comparison of results of brain scanning using ^{68}Ga-EDTA and the positron scintillation camera with ^{203}Hg-neohydrin and the conventional focused collimator scanner, Radiology 84 (1965) 502.

[8] SCHAER, L.R., ANGER, H.O., GOTTSCHALK, A., ^{68}Ga-EDTA experiences in brain lesion detection with the positron camera, J. Am. Med. Assoc. 198 (1966) 811.

[9] HAYES, R.L., CARLTON, J.E., BYRD, B.L., Bone scanning with gallium-68: a carrier effect, J. Nucl. Med. 6 (1965) 605.

[10] HAYES, R.L., "Radioisotopes of gallium," Ch. 33, Radioactive Pharmaceuticals (Andrews, G.A., Knisely, R.M., Wagner, H.N., Jr., Eds.), USAEC Conf-651111 (1966).

[11] WEBER, D.A., GREENBERG, E.J., DIMICK, A., KENNEY, P.J., ROTHSCHILD, E.O., MYERS, W.P.L., LAUGHLIN, J.S., Kinetics of radionuclides used for bone studies, J. Nucl. Med. 10 (1969) 8.

[12] EDWARDS, C.L., AHUMADA, J., HAYES, R.L., Skeletal Scanning with gallium-68 citrate, Oak Ridge Associated Universities, ORAU-101 (1966) 100.

[13] EDWARDS, C.L., HAYES, R.L., AHUMADA, J., KNISELY, R.M., Gallium-68 citrate: a clinically useful skeletal scanning agent, J. Nucl. Med. 7 (1966) 363.

[14] AHUMADA, J., HAYES, R.L., TANIDA, R., EDWARDS, C.L., Gallium-68 in bone scanning, Oak Ridge Institute of Nuclear Studies, ORINS-53 (1965) 85.

[15] BRUCER, M., ANDREWS, G.A., BRUNER, H.O., A study of gallium, Radiology 61 (1953) 534.

[16] HAYES, R.L., CARLTON, J.E., RAFTER, J.J., BYRD, B.L., Hydrous ferric oxide colloid labeled with gallium-68, Oak Ridge Associated Universities, ORAU-101 (1966) 78.

[17] HAYES, R.L., CARLTON, J.E., RAFTER, J.J., Scanning with hydrous ferric oxide colloid labeled with ^{68}Ga, J. Nucl. Med. 1 (1966) 335.

[18] KNISELY, R.M., EDWARDS, C.L., ANDREWS, G.A., TANIDA, R., HAYES, R.L., Bone marrow scanning with radioactive colloids, Oak Ridge Associated Universities, ORAU-101 (1966) 96.

[19] NELSON, B., HAYES, R.L., EDWARDS, C.L., Animal toxicity studies of a ferric oxide colloid suitable for marrow scanning, Oak Ridge Associated Universities, ORAU-101 (1966) 87.

[20] ANGHILERI, L., A new ^{68}Ga-compound for kidney scanning, Intl. J. Appl. Radiation Isotopes 19 (1968) 421.

[21] ANGHILERI, L., PRPIC, B., A new colloidal ^{68}Ga-compound for liver scanning, Intl. J. Appl. Radiation Isotopes 18 (1967) 734.

[22] EDWARDS, C.L., HAYES, R.L., Techniques to provide sterile and pyrogen-free radiopharmaceuticals from long-lived generators, Oak Ridge Associated Universities, ORAU-101 (1966), 83.

[23] HARTMAN, R.E., HAYES, R.L., Binding of gallium by blood serum, Oak Ridge Associated Universities, ORAU-101 (1966) 84.

[24] CHARKES, N.D., SKALAROFF, D.M., "The osseous system," Ch. 11, Clinical Scintillation Scanning (Freeman, L.M., Johnson, C.M., Eds.), Harper and Row (1969).

[25] COLOMBETTI, L.G., GOODWIN, D.A., ^{68}Ga-labeled macroaggregates for lung studies, J. Nucl. Med. 10 (1969) 328.

[26] ANGER, H.O., POWELL, M.R., VAN DYKE, D.C., SCHAER, L.R., FAWWAZ, R., YANO, Y., "Recent applications of the scintillation camera," Radioaktive Isotopen in Klinik und Forschung (Urban und Schwarzenberg, Muenchen, 1967).

Table I. Effect of carrier on 2-hr gallium
citrate distribution in the rat, expressed
as % of dose per gram of tissue (250-g rat)[a]

Tissue	Dose, mg Ga per kg body weight		
	C.F.[b]	1.0	10.0
Blood	1.33	0.59	0.10
Muscle	0.21	0.07	0.01
Kidney	0.42	1.51	4.27
Rib	1.61	2.96	3.35
Femur	1.20	2.15	2.41
Calvaria	0.65	1.28	1.50
Liver	0.29	0.21	0.08
Spleen	0.35	0.18	0.05
Lung	0.56	0.36	0.98
Animals	5	5	5

a. From Hayes, R.L., Radioactive Pharmaceuticals (1966) 606.

b. Carrier-free ^{68}Ga containing 1 mg of citric acid; other doses,
2:1 molar ratio of citrate to gallium.

Table II. Physical and chemical characteristics of bone tracers[a]

Nuclide	^{47}Ca	^{85}Sr	^{87m}Sr	^{18}F	^{68}Ga
Physical half-life	4.5 days	65 days	2.8 hr	110 min	68 min
Primary gamma energy (No./100 disintegrations)	1.31 MeV (76)	0.513 MeV (100)	0.388 MeV (78)	0.511 MeV (97,β+)	0.511 MeV (87,β+)
Chemical form	Chloride	Nitrate	Chloride	Sodium fluoride	Citrate + carrier Ga
Specific activity[b]	>140 mCi/gm Ca	>7 Ci/gm Sr	>5 Ci/gm Sr	Carrier free	Carrier free
Admin. activity	100 µCi	100 µCi	1 mCi	1 mCi	1 mCi[c]
Counts/min/µCi in std geom[d]	4.3 x 10³	1.01 x 10⁴	9.5 x 10³	1.96 x 10⁴	1.76 x 10⁴
Dose-to-bone (rads)	6.3[e]	5.2	0.14	0.26	0.38

a. From Weber, D.A., et al., J. Nucl. Medicine 10, 1969.
b. Specific activities listed refer to the time of injection.
c. Proposed dose.
d. 2-in.-diameter x 4-in.-long cylindrical bore collimator: Channel width = 100 keV, fixed source-to-crystal distance.
e. Includes dose from 5% contaminant of ^{45}Ca and ^{47}Sc daughter product of ^{47}Ca consequent on injecting 3 days post 7-day irradiation of ^{46}Ca.

Table III. Effect of dose on distribution of gallium-labeled
hydrous ferric oxide colloid in the rabbit[a]

| Tissue | Colloid dose (mg Fe per kg body wt) | | | |
	0.25	0.50	1.00	2.00
Percent injected dose/g[b]				
Liver	0.75 ± 0.05	0.83 ± 0.10	0.64 ± 0.02	0.56 ± 0.07
Marrow	0.90 ± 0.05	1.43 ± 0.16	1.46 ± 0.07	2.21 ± 0.11
Blood	0.003	0.005	0.003	0.054
Ratio Marrow to:				
Liver	1.22 ± 0.11	1.88 ± 0.31	2.34 ± 0.13	4.22 ± 0.55
Blood	300	400	490	65

Effect of stabilizer on distribution of gallium-labeled
hydrous ferric oxide colloid in the rabbit[a,c]

| Tissue | Amount dextran (mg/kg body wt) | | | |
	20	90	260	440
Percent injected dose/g[d]				
Liver	0.74 ± 0.06	0.63 ± 0.04	0.62 ± 0.02	0.61 ± 0.07
Marrow	0.69 ± 0.03	1.32 ± 0.08	1.23 ± 0.16	1.08 ± 0.12
Blood	0.014	0.003	0.006	0.007
Ratio Marrow to:				
Liver	0.94 ± 0.09	2.11 ± 0.17	2.00 ± 0.27	1.76 ± 0.27
Blood	120	440	230	110

a. From Hayes, R.L., et al., Hydrous Ferric Oxide Colloid Labelled
    with ^{68}Ga, ORAU-101 (1966) 80.
b. Normalized to 2.5 kg; average of five animals; killed 1 hr after
    intravenous administration.
c. 1 mg Fe/kg body wt., killed 1 hr after intravenous administration.
d. Normalized to 2.5 kg., average of five animals.

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