PHYSICAL CHEMISTRY 2008

Proceedings

of the 9th International Conference on Fundamental and Applied Aspects of Physical Chemistry

Volume II

The Conference is dedicated to the 200th Anniversary of the University in Belgrade

UNIVERSITY OF BELGRADE
1808 • 2008

September 24-26, 2008,
Belgrade, Serbia

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ISBN	978-86-82475-13-2
Title:	Physical Chemistry 2008. (Proceedings)
Editor:	Prof. dr A. Antić-Jovanović
Published by:	The Society of Physical Chemists of Serbia, Studentski trg 12-16, P.O.Box 137, 11001 Belgrade, Serbia
Publisher:	Society of Physical Chemists of Serbia
For publisher:	Prof. dr S. Anić, president of the Society of Physical Chemists of Serbia
Printed by:	"Jovan" Printing and Published Comp; 250 Copies; Number of Pages: x + 301 (469-770); Format B5; Printing finished in September 2008.
Text and Layout:	Aleksandar Nikolić

250 – copy printing

PHYSICO-CHEMICAL CHARACTERIZATION OF ^{90}Y-LABELED ANTIMONY TRISULFIDE COLLOID AND COMPARISON WITH ^{99m}Tc-LABELED ONE

D. Janković, D. Đokić and N. Nikolić

Vinča Institute of Nuclear Sciences, 11000 Belgrade, Serbia

Abstract

In radionuclide therapy, the importance of ^{90}Y as a beta-emitting radionuclide is increasing rapidly. The properties of the ^{90}Y-labeled antimony trisulfide colloid (Sb_2S_3) were compared with the ^{99m}Tc-labeled one. Labeling efficiencies reached >96% and >97% for ^{90}Y- and ^{99m}Tc-labeled colloids respectively. Both preparations were stable for 72 h in saline and 1% albumin solution. Filtration analysis showed that more than 94% of total ^{90}Y radioactivity is associated with the colloidal particles smaller than 20 nm, while more than 90% of ^{99m}Tc radioactivity is associated with the particles retained on the filter with a 20 nm pore size. ^{90}Y-labeled colloids showed high labeling efficiency, stability and potency for clinical use.

Introduction

During the last decade there has been an increased interest in the application of radiopharmaceuticals in the direct management of serious illnesses, especially various forms of cancer and rheumatism. Yttrium-90 (^{90}Y) is a clinically acceptable β-emitting radionuclide, useful for therapy. It is a pure beta emitter, with a half-life of 64.4 hours, $E_{max\beta-}$ of 2.27 MeV and also has a lack of gamma radiation, and these characteristics of ^{90}Y make it a good choice for safe patient treatments. ^{90}Y is obtained from ^{90}Sr as a high yielded fission product [1].

Radiocolloids play an important role as diagnostic and therapeutic agents in nuclear medicine. The properties of radiocolloid dispersion, characterized by particle size, shape, charge and stability, are significant parameters which determinate its organ distribution *in vivo*.

^{99m}Tc-antimony trisulfide colloid has been used for bone marrow imaging, lymphedema assessment, and more recently, for scintigraphic mapping of lymphatic channels and sentinel nodes in melanoma and breast cancer [2, 3]. Its particles have been reported to range from 3 to 30 nm, which is an optimum size for imaging lymphatic channels in lymphoscintigraphy. The aim of this study was to investigate the labeling and stability of ^{90}Y-antimony trisulfide colloid particles.

Experimental

$^{90}YCl_3$ was purchased from Polatom, Poland. ^{99m}Tc-pertechnetate was obtained from a ^{99}Mo/^{99m}Tc radionuclide generator (INS Vinca, Belgrade). *Antimony sulfide colloid* was prepared by saturating 100 ml of boiled water for injection with hydrogen sulfide gas for 1 h. Twenty milliliters of 1% aqueous solution of antimony potassium tartrate (Merck,) were added and after the mixing an orange

liquid was obtained. In the next step 10 ml of a 4.0% aqueous solution of polyvinylpyrrolidone (povidone, PVP, average M_w ca. 44,000, Fluka) were added and an excess of hydrogen sulfide was removed by purging with nitrogen gas for 30 min. Absence of hydrogen sulfide was confirmed with lead acetate paper. The preparation was then divided into aliquots of 2 ml and sterilized by membrane filtration (220 nm) into sterile reaction vials and storage in a refrigerator. Right before the adding of $^{90}YCl_3$, pH of the colloid solutions was adjusted to a desired value (1.5, 3.0 and 5.0). ^{90}Y-antimony sulfide was then prepared by adding 5-10 μl of $^{90}YCl_3$ stock solution (~185 MBq). The mixture was kept at room temperature for different times or heated in a boiling-water bath for 30 min and then left to cool at room temperature. The ^{99m}Tc-labelled colloid was prepared in the same manner as reported for the ^{90}Y-labelled one.

Radiochemical purity of the ^{90}Y-labeled colloid was evaluated by using Whatman-3 paper strips and developed in a solvents mixture of pyridine, ethanol and water with a volume ratio of 1:2:4 respectively. Labeling efficiency of the ^{99m}Tc-labeled colloid was checked by the ITLC-SG/ acetone system.

To check the stability, the particles of ^{90}Y and ^{99m}Tc-labeled colloids were incubated in a saline and 1% albumin solution and the mixture was agitated at 37 °C for 72 hours. At different points in time, the particles were centrifuged, separated from the liquid phase and counted to estimate the extent of leaching of the activity from them.

Filtration analysis. Sterile filters: Whatman (20-100 nm) and Millipore (220 nm) were used for particle size analysis.

Results and Discussion

The radiolabeling yield of the ^{90}Y-antimony trisulfide colloid was dependant on the reaction temperature as well as the pH value. The results of labeling studies with this colloid at various pH values and temperatures are given in Fig. 1 as mean value of 3 radiolabeling probes (n=3). Studies on the effect of temperature showed that the labeling was low at room temperature (RT), with the yield being < 50% for a reaction time of 2 h at a pH value of 1.5. The maximum labeling yield of 96.8% ± 1.2% could be obtained when the labeling was carried out at a pH value of approximately 1.5 and at a reaction temperature of 95 ^{o}C for 30 min. Since the highest labeling yield was observed at these conditions, the following stages of the study were carried out with this formulation. The radiochemical purity of ^{99m}Tc-antimony trisulfide prepared in these conditions was found to be higher than 97%.

The stability of ^{90}Y- and ^{99m}Tc-labeled Sb_2S_3 colloid in a saline and 1% albumin solution was assessed by measuring the release of ^{90}Y and ^{99m}Tc from the particles at 37 °C up to 72 hours. The ^{90}Y-antimony trisulfide colloid was quite stable, confirming that the metal remained bound to the colloid. During 72 h of incubation in saline and 1% albumin solution approximately <1.0% and <1.5% of ^{90}Y were released respectively. The ^{99m}Tc-antimony trisulfide colloid was also stable in vitro, showing >2% and >3.0% releases of the radionuclide during 72 h of incubation in saline and 1% albumin solution, respectively.

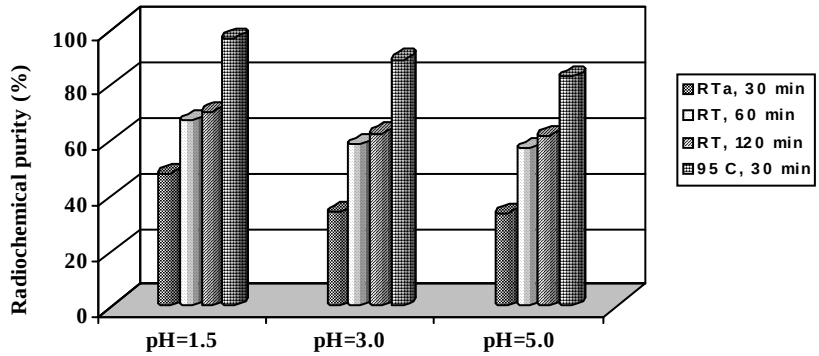

Fig 1. The labeling yield of ^{90}Y-antimony trisulfide in different reaction conditions (mean, n=3)

The results of filtration analysis showed that more than 94% of the total ^{90}Y radioactivity is associated with the antimony trisulfide colloid particles smaller than 20 nm, while more than 90% of ^{99m}Tc radioactivity is associated with the particles retained on the filter with pore size of 20 nm (Table 1).

Table 1. Radioactive particle size distribution

Filter pore size / Colloids	% Activity retained (mean ± SD)			
	0.22 μm	0.1 μm	0.05 μm	0.02 μm
^{90}Y- Sb_2S_3	-	-	-	5.9±2.1
^{99m}Tc- Sb_2S_3	-	-	5.3±0.8	90.7±2.2

Conclusion

The antimony trisulfide colloid particles used in this study appear to be very well suited for labeling with beta emitting radionuclides. This colloid can be prepared from common chemicals and can be formed into particles of a desired size range using a controlled process. Radiolabeling of this colloid with ^{90}Y is simple to perform and provides a very high yield. The ^{90}Y-antimony trisulfide colloid demonstrates high *in vitro* stability in either saline or 1% albumin solution at 37 ^{o}C up to 72 h.

Acknowledgments

The research work has been financially supported by the Ministry of Sciences of the Republic of Serbia, Grant No. 142051.

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