



⁹⁰Y-labeled Antimony Trisulfide Colloid as Promising Therapeutic Agent: Physicochemical Characterization and Biological Evaluation

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SUMMARY

Introduction The suitability of ⁹⁰Y-labeled antimony trisulfide colloid (ATC) for the preparation of therapeutic radiopharmaceutical was studied taking into accounts its physicochemical properties and biological behavior in rats.

Material and methods The labeling efficiency of ⁹⁰Y- and ^{99m}Tc-labeled colloid particles was investigated by ITLC-SG and paper chromatography, the *in vitro* stability of the colloid was tested in human serum, while *in vivo* experiments were performed on healthy Wistar rats. Analysis of the particles enclosed the size (TEM), determination of the zeta potential (Zetasizer Nano) as well as radioactivity particle size distribution (filtration analysis).

Results ⁹⁰Y-labeled ATC can be prepared in high yield under investigated conditions. Labeling efficiency was >95% and filtration analysis showed that more than 90% of radioactive particles were smaller than 20 nm. The particles with the size range of 6-22 nm were achieved by using polyvinylpyrrolidone (mol wt ~44,000). The ⁹⁰Y-ATC was quite stable *in vitro* in human serum. Tissue distribution studies in rats confirmed that the liver and spleen uptake of ⁹⁰Y-labeled colloid was three-fold lower in comparison with ^{99m}Tc-ATC, although the bone uptake was five-fold higher at 20 min post injection.

Conclusions ⁹⁰Y-labeled ATC showed high labeling efficiency and good stability, and might be well suited for therapeutic application in nuclear medicine.

Keywords: yttrium-90; radiocolloid; particle size; labeling; tumor therapy

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INTRODUCTION

The main purpose of radiopharmacology is to study the chemical properties of radiopharmaceuticals and their interactions with living organisms. Radiopharmaceuticals are used in the field of nuclear medicine as tracers in the diagnosis and treatment of many diseases.

Therapeutic radiopharmaceuticals are radiolabeled molecules designed to deliver therapeutic doses of ionizing radiation to specific disease sites (most often cancerous tumors) with high specificity in the body. Because of the multiple parameters that must be considered, developing effective radiotherapeutic drugs is a complex problem that is not simply accomplished by attaching a radionuclide. The physical half-life is a critical consideration in the design of therapeutic radiopharmaceuticals.

For systemic cancer radiotherapy, yttrium-90 (⁹⁰Y) is a clinically acceptable β-emitting radionuclide. It is a pure beta emitter with high energy ($E_{\max} \beta$ of 2.27 MeV) and with a half-life of 64.4 hours which is short enough to achieve a critical dose rate and long enough to allow the radiopharmaceutical to be manufactured and delivered for clinic use. Also, yttrium-90 is a long-ranged radionuclide with maximum tissue penetration of nearly 1 cm with 80% of the energy deposited in the first 4 to 5 mm. ⁹⁰Y is obtained from ⁹⁰Sr as a high yielded fission product [1].

Radiocolloids, as diagnostic and therapeutic agents, play an important role in nuclear medicine. The properties of radiocolloid dispersion, characterized by particle size, shape, charge and stability, are very significant parameters that determine its organ distribution *in vivo* [2-5]. Uptake of colloids of similar size can vary substantially. Differences in surface characteristics of the colloids may account for these observations [6]. In rats, for instance, small, negatively charged liposomes localize more effectively in lymph nodes than positively charged vesicles [7].

Colloidal particles smaller than a few nanometers usually leak into blood capillaries, whereas larger particles (up to 100 nm) can penetrate in the lymphatic capillaries and are trapped in the bone marrow [8]. The optimal colloidal size for lymphoscintigraphy is believed to be approximately 50–70 nm [9]. Individual estimation varies from 1 to 70 nm [3].

^{99m}Tc-ATC 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 [10-18]. Its particles have been reported to range from 3 to 30 nm, an optimum size for imaging lymphatic channels in lymphoscintigraphy [19, 20].

THE AIM

The goal of this study was to prepare labeled antimony trisulfide colloid with ⁹⁰Y and explore the potential for regional radiotherapy against malignant solid tumors. The preparation was studied for its stability, labeling yield and biological efficacy. The results obtained were compared of the corresponding ^{99m}Tc-labeled one.

MATERIAL AND METHODS

Carrier free ⁹⁰Y in the form of yttrium chloride was purchased from Polatom, Poland. ^{99m}Tc-pertechnetate was obtained by a ⁹⁹Mo/^{99m}Tc radionuclide generator (Vinča Institute of Nuclear Sciences, Belgrade, Serbia). All other reagents and solvents used in these studies, purchased from commercial sources, were used without further purification.

Optimization studies for the preparation of ⁹⁰Y-labeled colloid

Antimony trisulfide colloid (ATC) 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, Darmstadt, Germany) were added and after mixing an orange liquid was obtained. The solution obtained was divided into three equal parts in separate vials and then, 3.5 mL of 4.0% aqueous solution of polyvinylpyrrolidone (PVP, Sigma-Aldrich, USA) with mol wt ~10,000; 44,000 and 360,000 were added in each part respectively. An excess of hydrogen sulfide was removed by purging with nitrogen gas for 30 min. Absence of hydrogen sulfide was confirmed by using lead acetate paper. Two-milliliter aliquots of the resultant preparation were then dispensed and sterilized by membrane filtration (0.22 μm) into sterile reaction vials under nitrogen environment and stored in a refrigerator until use. Antimony colloid stabilized with PVP of mol wt ~10,000; 44,000 and

360,000 were designated as ATC-10, ATC-44, and ATC-360, respectively.

2 μL of $^{90}\text{YCl}_3$ stock solution (~ 37 MBq) in 0.5M HCl was added to 2.0 mL of the preformed antimony trisulfide reagent in a 10-mL reaction vial, followed by 0.2 mL of 1.0 M HCl. Final pH value of the mixture was 1.5. The mixture was kept at room temperature for different time or heated for 30 min at 50 and 95 $^{\circ}\text{C}$ and then cooling to room temperature. Then, 0.5 mL of sodium acetate buffer was added to bring the pH value to 6.2-6.6.

Preparation of $^{99\text{m}}\text{Tc-ATC}$

18.5 MBq of sodium pertechnetate ($^{99\text{m}}\text{TcO}_4^-$) was added to vials containing antimony trisulfide colloid. $^{99\text{m}}\text{Tc}$ -labeled colloid was prepared in the same manner as that reported for yttrium-90 labeled one.

Transmission electron microscopy (TEM)

The samples were spotted on to plastic-coated (carbon-stabilized) copper grids (300 mesh) and allowed to partially dry in air. The grid was washed with sterile distilled water to remove any water-soluble salts. The samples were examined using a transmission electron microscope (TEM, Philips EM 400T microscope with the operating voltage of 120 kV).

Quality control of ^{90}Y and $^{99\text{m}}\text{Tc}$ -labeled ATC

Radiochemical purity of ^{90}Y -labeled ATC was evaluated by using paper chromatography system. Approximately 5 μL of sample was applied to Whatman-3 paper strips (Gelman Science, Ann Arbor, MI, USA) and developed in a 1:2:4 solvents mixture of pyridine, ethanol and water used as a mobile phase. In these conditions, the labeled colloid remained at the origin ($R_f=0$), while unbound ^{90}Y migrated with the solvent front, $R_f=1$.

Labeling efficiency of $^{99\text{m}}\text{Tc}$ -labeled ATC was performed using ascending instant TLC with a silica gel-impregnated glass fiber strip (ITLC-SG; 1 x 16 cm; Gelman Sciences) and acetone as a mobile phase. The labeled colloid remained at the origin while pertechnetate migrated with the solvent front to R_f of 1.0.

In vitro stability studies

The stability of ^{90}Y -labeled ATC, stored in a refrigerator at 4°C , was evaluated for a period of up to 72 h by chromatographically measuring their radiochemical purity at different times

after preparation. The radioactivity was monitored by a Capintec CRC-15 beta dose calibrator (Capintec, INC., New Jersey, USA).

To check the stability in body fluid, the particles of labeled colloid were incubated in human serum at 37°C for 10 days. Human serum was prepared by allowing blood collected from a healthy volunteer to clot 1 hr at room temperature in a closed tube. The sample was centrifuged and the supernatant serum was transferred to sterile plastic culture tubes. It was then incubated overnight at 37°C in a humidified 5% carbon dioxide, 95% air atmosphere. The pH value of an aliquot was measured as 7.4 before the addition of ^{90}Y -radiolabeled ATC and maintained at pH value 7.4 ± 0.1 throughout the experiment. In triplicate, 100 μL of labeled ATC was then added to 2.0 mL of serum and then returned to incubate at 37°C in a CO_2 -enriched atmosphere (5% CO_2). At different points of time (1, 2, 4, 6, 12 hours and 1, 2, 3, 5, 7, 10 days), the particles were centrifuged, separated from the liquid phase and counted to estimate the extent of leaching of the activity from them.

Radioactive particle size and charge (zeta potential) distribution

Filtration analysis. Sterile filters: Whatman 0.02-0.1 μm (International Ltd) and 0.22-1.0 μm (Millipore Co. Bedford, Ma. USA) were used for particle size analyses. All filters were preequilibrated with an initial wash of saline (1.0 mL) and finally rinsed with saline (2.0 mL) after filtration followed by approximately 5 mL of air to ensure complete filtration. A radiocolloid sample (0.1 mL) was taken from the reaction vial and filtered through a 0.22- μm filter. The filter was rinsed and then the filter and the obtained filtrate were counted separately in a validated counting unit CRC-15 beta. A radiocolloid sample (0.1 mL) was taken from the previous filtrate, filtered through a 0.1 μm filter, and rinsed. Both, the filter and the filtrate were counted. The process was repeated for 0.05, 0.03 and 0.02 μm filters. All values were corrected for background. Each experiment was performed in triplicate.

Zeta potential analysis. To determine the zeta potential (surface charge), Y-ATC was prepared using nonradioactive yttrium chloride and keeping the amount of yttrium identical to those in radioactive preparation. In tech-

netium preparation, it was used radioactive ^{99m}Tc. The zeta potential of labeled ATC was measured using a light-scattering photon correlation spectroscopy (PCS) instrument Zetasizer Nano ZS (Malvern Instruments Ltd., Malvern, England, U.K.) by “size and zeta potential” folded capillary cell (DTS 1060). The pH values of the samples were 6.2-6.4. Values reported are the mean ± standard deviation of at least three different batches.

Biological distribution studies of ⁹⁰Y and ^{99m}Tc-labeled colloid

In vivo distribution studies of ⁹⁰Y and ^{99m}Tc-labeled colloid were carried out in healthy Wistar rats (female, four weeks old, average weight about 100 g). The 0.1 mL of labeled colloid (~1.4 MBq and 0.74 MBq of ⁹⁰Y and ^{99m}Tc-labeled colloid, respectively) was injected into the tail vein. The rats were sacrificed at different times post injection (20 min and 24 h). Samples of blood and organs were taken and weighed, and the radioactivity was counted on a NaI (Tl) well counter. The counting was carried out under the same geometric conditions. All samples were made up to a 1 mL volume with water to establish a linear relationship between the counting rate and the sample size. Raw radioactivity data was corrected for background and tested for quantification limits according to literature [21]. The %ID/g of each organ and blood were calculated by comparing their activities with the appropriate standards for injected dose (ID). The entire animal study conformed to ethical guidelines and complied with the United Kingdom Biotechnology and Biological Sciences Research Council's Guidelines on the Use of Living Animals in Scientific Investigations.

Statistical analyses

The results are reported as mean ± standard deviation. Student's t-tests or analysis of variance (ANOVA) were used for comparisons between two groups. Statistical significance difference was defined as a p value of less than 0.05.

RESULTS

Particle size

Particle size distributions of ⁹⁰Y-ATC and ^{99m}Tc-ATC preparations are shown in Figure 1. ⁹⁰Y-ATC prepared using PVP of mol wt ~44,000 (ATC-44) has a curve of particle size

distribution with a single peak with a 14 nm diameter and range of 6-22 nm. In contrast, the distribution curve of colloid prepared with PVP of mol wt ~360,000 (ATC-360) does not have a single definite peak, but has several minor peaks spread across a size range from 6 to 26 nm. ⁹⁰Y-ATC prepared with PVP of mol wt ~10,000 (ATC-10) precipitated when heating (at 50°C and 95°C for 30 min) during the labeling procedure, while without heating resulted in poor labeling efficiency. Further studies of ATC-10 were therefore abandoned. The distribution curve of ^{99m}Tc-ATC prepared with PVP of mol wt ~44,000 has a single definite peak at 26 nm diameter and range of 10-36 nm. As ⁹⁰Y-ATC particles prepared using PVP of mol wt ~44,000 were visualized as spherical by TEM and has a curve of particle size distribution with a single peak, further studies were carried out with this formulation.

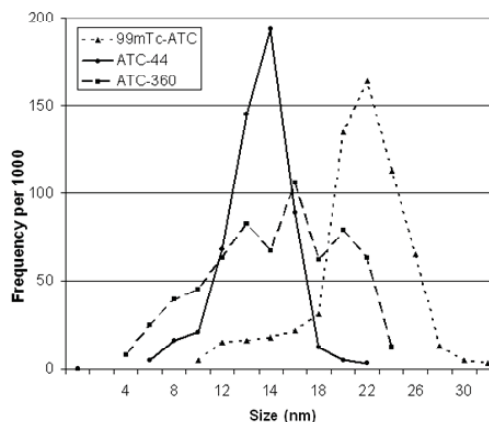


Figure 1. Particle size distribution of ⁹⁰Y-ATC stabilized with PVP of mol wt 44,000 (ATC-44) and 360,000 (ATC-360), compared to ^{99m}Tc-ATC stabilized with PVP of mol wt 44,000

Radiolabeling

The effect of temperature on the percentage of ⁹⁰Y-ATC yield was shown in Table 1. It could be observed that the labeling yield increases with an increase in temperature. The yield, analyzed by paper chromatography, was found to be higher at 95°C for 30 min in a boiling water bath (96.4 ± 1.2%), than at 50°C for 30 min (88.1 ± 1.8%) or at room temperature for 240 min (65.9 ± 1.6%). Since the highest labeling yield was observed by heating at 95°C for 30 min of acidified ATC (pH 1.5), the following stages of the study were carried out with this formulation.

	Temperature	Value (mean±SD)
Room temperature	30 minutes	37.6±1.3
	60 minutes	61.3±1.4
	240 minutes	65.9±1.6
Heating for 30 minutes	50 °C	88.1±1.8
	95 °C	96.4±1.2

Table 1. Influence of temperature on labeling yield of ⁹⁰Y-ATC (n=5)

Figure 2. In vitro stability of ⁹⁰Y-ATC

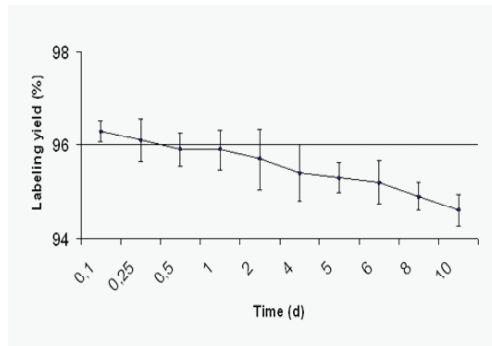


Figure 3. Biological behavior of ⁹⁰YCl₃, pH=6.0 (values reported are as %ID/g, n=3-5)

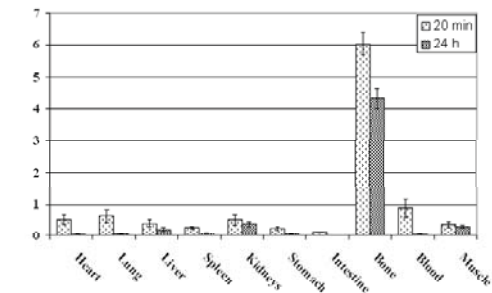


Figure 4. Biological behavior of ^{99m}Tc-ATC, pH=6 (values reported are as %ID/g, n=3-5)

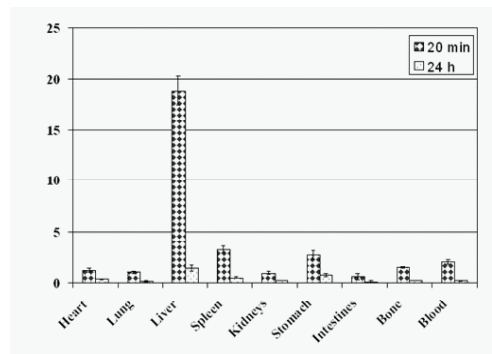


Figure 5. Organ uptake study of ⁹⁰Y-ATC in health Wistar rats (%ID/g, n=3-5)

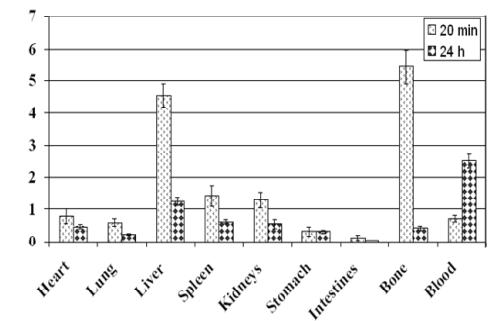


Table 2. Percent retention of radiolabeled colloid filtered through filters with different pore size

Pore size (nm)	% activity retained on filter				n
	⁹⁰ Y-ATC		^{99m} Tc-ATC		
	Fresh	5 days old	Fresh	5 days old	
100	-	-	-	-	3
50	-	-	1.25±0.31	1.36±0.23	3
30	3.41±0.52	3.89±0.35	16.21±1.11	16.01±0.81	6
20	5.89±1.05	6.15±0.65	63.75±2.36	64.15±1.78	6

Results are expressed as mean values ± SD.

In vitro stability study

In stability experiments, no significantly detectable dissociation of yttrium-90 radiolabeled colloid, stored in a refrigerator at 4°C for 72 h, was observed, confirming that the metal remained bound to the colloid. The stability of ⁹⁰Y-labeled colloid in human serum was assessed by measuring the release of ⁹⁰Y from the particles up to 10 days. The ⁹⁰Y-ATC was quite stable, because < 2% of radionuclide was released during 10 days of incubation. The results are shown in Figure 2 as ⁹⁰Y radioactivity was retained within the particles during incubation time.

Radioactive particle size distribution and zeta potential

The results of the radioactive particle size distribution studies by filtration are given in Table 2. Under the investigated conditions more than 90% of the ⁹⁰Y-activity was found to be associated with the particles less than 20 nm in size. In the case of ^{99m}Tc-ATC, 63.75%, 16.21% and 1.25 % of the total radioactive particles are larger than 20, 30 and 50 nm, respectively.

Under the well-standardized conditions of the preparation of ATC, the reproducibility of the radioactivity particle size distribution was good. The particle size stability studies of ⁹⁰Y and ^{99m}Tc-ATC demonstrated that there were no significant changes in particle size distribution over the 5 days study period (p>0.05).

The results of zeta potential measurements reveal that Y-ATC prepared using PVP of mol wt ~44,000 and 360,000 exhibited negative zeta potential values of -19.3±0.3 mV and of -3.3±0.2 mV respectively. For ^{99m}Tc-ATC particles prepared using PVP of mol wt ~44,000 the zeta potential value was of -7.1±0.4 mV.

Biological distribution studies

Biodistribution studies of ⁹⁰YCl₃ were carried out and the obtained results are presented in Figure 3. The uptake in all organs was expressed as the radioactivity observed in those

organs per gram. The values of 6.02% and 4.13%/g of the injected activity was observed in bone (femur) at 20 min and 24 h post injection, respectively. The uptake in other organs at 24 h post injection was significantly lower than at 20 min ($p < 0.05$). The results indicate longer retention of ⁹⁰Y in the femur; the blood radioactivity was completely cleared within twenty-four hours post injection, but there was a very slow clearing of radioactivity from the muscle.

Figure 4 shows the biodistribution of ^{99m}Tc-ATC in rats at 20 min and 24 h after intravenous injection. After 20 min from injection, most of the injected colloid was found in the liver, spleen and blood, compared with lower uptake by other organs. A significant decrease in whole body activity (corrected for physical decay of ^{99m}Tc) was obtained at 24 h ($p < 0.05$).

Compared to ⁹⁰YCl₃ and ^{99m}Tc-ATC, ⁹⁰Y-ATC showed much different biological behavior (Figure 5). The uptake of ⁹⁰Y-labeled colloid in the liver and spleen was significantly lower compared to the values obtained for ^{99m}Tc-labeled one at 20 min p.i. ($p < 0.05$). ⁹⁰Y-labeled colloid showed higher uptake in bone at 20 min p.i. but had a much lower level at 24 h p.i. ($p < 0.05$). In the heart, lung, liver, spleen, kidneys and intestines, the radioactivity significantly decreased at 24 h, while an increased uptake in the blood was observed at 24 h p.i. In other organs, much lower radioactivity was detected at 24 h p.i. ($p < 0.05$).

DISCUSSION

There is a class of ^{99m}Tc radiopharmaceutical colloids that is used to assess the state of the disease or the function in patients by taking advantage of the biological distribution of these particles in vivo. The particle size, shape and charge determine the biological behavior of radiocolloid. The particles larger than 10-15 μm (but <100 μm) are trapped in lung capillaries by a purely mechanical process, and thereby can be used to evaluate pulmonary lung perfusion. Particles below 1-10 μm in size are taken up by the reticuloendothelial system of the liver (primarily 0.3-1 μm particles), spleen (mainly >1 μm particles), and bone marrow (predominantly <0.1 μm particles) [22].

The ATC particles used in this study appear to be very attractive for labeling with beta emitting radionuclides. This colloid can

be prepared from common chemicals and can formed particles of a desired size range in a controlled process.

In our previous paper, we compared and evaluated three various sizing techniques (PCS, TEM and filtration analysis) for ⁹⁰Y-labelled ATC and Sn colloid and concluded that differences found among PCS and TEM results. Significantly different mean diameters of the colloid particles were found by these techniques. TEM has an excellent resolution necessary for radiocolloid particle-sizing analysis, and it is a desirable size-measuring technique because it is more reliable than PCS [23].

Polyvinylpyrrolidone of mol wt ~44,000 is added to stabilize the colloid. Our previous investigations had shown that the absence of PVP had resulted in the aggregation and settling of the colloidal preparation. PVP of mol wt ~44,000 appears to be better than PVP of different mol wt (10,000 and 360,000) for stabilizing the colloid. These results are in accordance with the literature data for ^{99m}Tc-ATC [18].

To accelerate the binding of yttrium to the colloid, hydrochloric acid is added and the preparation is heated at 95°C. The optimum pH value for labeling was found to be approximately 1.5. Because, our unpublished investigation had shown that the labeling yield significantly decreased with the increase in pH value during labeling (from pH=3.0 to pH=6.0). The labeling yield increased with an increase in temperature, the optimum temperature was found to be at 95°C for 30 min.

The ⁹⁰Y-ATC demonstrates high *in vitro* stability either stored in a refrigerator at 4°C for 3 days or in human serum at 37°C up to 10 days.

A more rapid technique for measuring radioactive particle size distribution is filtration. The principle of size measurement for this technique is based on d_v . These experiments showed that in the case of antimony trisulfide colloid, more than 90% of the total ⁹⁰Y radioactivity is associated with the colloidal particles smaller than 20 nm, while more than 80% of ^{99m}Tc radioactivity is associated with the particles retained on the filter with pore size of 20 nm. These findings are in agreement with TEM observations.

Erroneous results such as overestimation of particle percentage due to non-specific retention on the filter may be obtained when the colloid particles are evaluated by filtra-

tion analysis. Therefore, the filters with well-defined pores were used, because many studies from literature have shown a preference of these filters for measurement of ^{99m}Tc -ATC particles size distribution [24].

The biodistribution and final fate of intravenously injected colloids is highly dependent on their particle size and surface charge. According literature data positively charged colloid particles sized in the micrometer range are quickly taken out of the blood pool by the reticuloendothelial cells of the liver and spleen [25]. Particles smaller than $0.1\ \mu\text{m}$ are able to pass the fenestration in the liver and may be able to target the hepatocytes, although most are still taken up by the liver's Kupffer cells. Negatively charged or neutral particles can evade this fast uptake and circulate in the blood system for several days [25]. The results of zeta potential measurements of Y-ATC particles showed that they were a negatively charged. Polyvinylpyrrolidone, as a stabilizer, had influenced the zeta potential in Y-ATC particles. The role of particle zeta potential in influencing biodistribution of radiocolloid was not investigated in this study. Measurement of zeta potential was performed only *in vitro* with formulations where PVP of mol wt $\sim 44,000$ and $360,000$ were used, but the definitive determination must be made *in vivo* to assess the effect of interaction with plasma proteins.

Most of ^{99m}Tc -ATC radioactivity that was injected intravenously in rat was trapped in the liver and spleen. A significant increase in bone and a decrease in liver and spleen uptake of ^{90}Y labeled ATC particles were observed contrary to the findings for ^{99m}Tc labeled colloid particles. It was speculated that the change in biological behavior of ^{90}Y and ^{99m}Tc labeled colloid was due to changes in particle size distribution and zeta potential. As the particle surface properties may influence the uptake of colloid, it was also supposed that the small size and negative charge of ^{90}Y labeled colloid particles were the cause why they weren't phagocytosed selectively by the reticuloendothelial system of liver and spleen. But they were small enough to be taken up by bone marrow.

To evaluate the efficiency of the ^{90}Y labeled colloid particles a comparison between biodistribution study results of ^{90}Y labeled colloid and $^{90}\text{YCl}_3$ was made. These results indicate that the percent of bone uptake per g for $^{90}\text{YCl}_3$ and ^{90}Y -ATC was similar. When $^{90}\text{Y(III)}$

chloride is injected into a rat, yttrium-90 is deposited in the bone. The level of yttrium-90 in bone slowly decreased with time (24 h). However, a considerable difference in deposition of the ^{90}Y -labeled colloid particles in rats was observed. The biodistribution data show a significant amount of accumulated ^{90}Y -labeled colloid particles in the bone tissue at 20 min p.i., while a significant decrease in bone radioactivity was detected at 24 h post injection. Thereafter the radiolabeled colloid is washed out from the bone tissue at a much faster rate than that observed in the case of $^{90}\text{YCl}_3$. The radioactivity from ^{90}Y -labeled colloid particles in the blood was significantly increased within 24 h post injection compared with $^{90}\text{YCl}_3$.

CONCLUSIONS

These experimental studies showed that under well-standardized conditions of the preparation of ^{90}Y -ATC, the reproducibility of the particle size and its distribution is very good. A promising preliminary result of the *in vivo* experiments suggests that ^{90}Y -ATC may be useful for therapeutic purposes in nuclear medicine. Further investigation has to be made on localization of this ^{90}Y -labeled ATC in tumor bearing rats.

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Obeležavanje antimon trisulfid koloida itrijumom-90 za primenu u terapiji: fizičko-hemijska karakterizacija i biološko ponašanje

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KRATAK SADRŽAJ

Uvod Cilj ovog rada je ispitivanje uslova i mogućnosti obeležavanja antimon trisulfid koloida (ATC) itrijumom-90 za pripremu terapijskog radiofarmaceutika uzimajući u obzir njegove fizičko-hemijske osobine i biološko ponašanje u pacova.

Materijal i metode Efikasnost obeležavanja koloidnih čestica itrijumom-90 i tehnecijom-99m je ispitivana hromatografijom na tankom sloju (ITLC-SG) i hromatografijom na hartiji. *In vitro* stabilnost obeleženog koloida je ispitivana u humanom serumu, dok je biodistribucija praćena po organima oglednih životinja (Wistar beli pacovi). Veličina obeleženih čestica je određivana transmissionom elektronskom mikroskopijom (TEM), dok je za zeta potencijal korišćen Zetasizer Nano, a filtraciona analiza za raspodelu radioaktivnih čestica po veličini..

Rezultati Antimon trisulfid koloid je obeležen itrijumom-90 u visokom prinosu pod ispitivanim uslovima. Efikasnost obeležavanja je bila veća od 95%, a veličina preko 90% obeleženih čestica je bila manja od 20 nm. Čestice opsega veličina od 6-22 nm su dobijene korišćenjem polivinilpirolidona molekulske mase ~44,000. ⁹⁰Y-ATC je stabilan *in vitro* u humanom serumu u toku 10 dana. Ispitivanje biodistribucije kod pacova je potvrdilo da je nakupljanje ⁹⁰Y-obeleženog koloida u jetri i slezini tri puta manje u poređenju sa ^{99m}Tc-ATC, iako je nakupljanje u kostima pet puta veće 20 minuta nakon injiciranja.

Zaključak Visoka efikasnost obeležavanja i stabilnost ⁹⁰Y-ATC ga čini pogodnim za terapijsku primenu u nuklearnoj medicini.

Ključne reči: itrijum-90; radiokoloid; veličina čestica; obeležavanje; terapija tumora

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