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The applicability of DTPA derivative for renal function diagnosis and intravascular brachytherapy

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1. Introduction

Brachytherapy is the one of the effective treatments for in-stent restenosis. The radioactive-liquid filled balloon using rhenium(Re-188/186) for brachytherapy requires that the form of radioactive compound ensure rapid excretion via the urinary system without any localization in blood and other organs and the dose to critical organs to be minimal in case of balloon rupture.

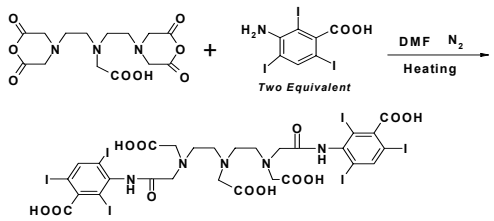
In this investigation, we synthesized a DTPA derivative (DTPA-ATBA) containing iodine and prepared ^{99m}Tc-(DTPA-ATBA) [1,2]. Also, to minimize the radiation risk of rhenium based liquid radiation sources in the event of balloon rupture, the ^{99m}Tc-(DTPA-ATBA) was estimated with results of image scans of the rabbit as viable substitutes for Re-188/186 compound in radioactive liquid-filled balloon for intravascular radiation therapy and renal function diagnosis [3,4].

Therefore ^{188}Re-DTPA complex will be a good alternative not only to see if the balloon has close contact with the blood vessel wall for the delivery of a sufficient radiation dose to the stenotic artery, but also to realize an early detection of a leakage in the worse case scenario of a balloon's rupture.

2. Methods and Results

2.1 Synthesis of DTPA- ATBA

The DTPA bisamide derivative, DTPA-ATBA (3-amino-2,4,6-triiodobenzoic acid), was synthesized by the reaction of DTPA dianhydride freshly prepared *in situ* by using acetic anhydride with 3-amino-2,4,6-triiodobenzoic acid as given in Scheme 1.



Scheme 1. Chemical structure of DTPA-ATBA

2.2 Preparation of ^{99m}Tc-(DTPA-ATBA)

[^{99m}Tc] pertechnetate was reacted with DTPA-ATBA (20mg) in the presence of stannous(II) chloride ($SnCl_2 \cdot 2H_2O$, 0.4mg) resulting in the formation of ^{99m}Tc -(DTPA-ATBA). To optimize the radiorableling efficiency of ^{99m}Tc-(DTPA-ATBA), two ^{99m}Tc-complexes were prepared at the different pH of 4 and 6, respectively. The radiolabeling yield was determined by using an ITLC scanner using silica alumina impregnated glass fiber sheets. (Fig.1)

The radiolabeling efficiency of ^{99m}Tc-(DTPA-ATBA) was maintained with high radiochemical purity (>98%) at room temperature for 6 h.

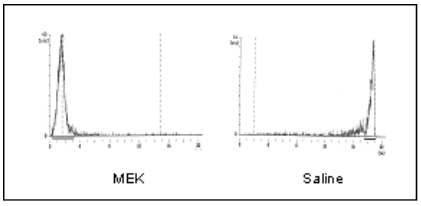


Fig. 1 The ITLC pattern of the ^{99m}Tc-(DTPA-ATBA)

2.3 Animal study

To examine the *in-vivo* retention of ^{99m}Tc-(DTPA-

ATBA), male New Zealand white rabbits were used. Each rabbit was injected with the ^{99m}Tc-(DTPA-ATBA) via the left ear vein. To confirm the dynamic kinetics of the ^{99m}Tc-(DTPA-ATBA), whole-body dynamic images and time-radioactivity curves of the kidneys for 30 min using a gamma camera were obtained. The results are described in Fig.2 at the different pH of 4 and 6.

The serial static image scans of the rabbit administered with the ^{99m}Tc-(DTPA-ATBA) revealed that none of the tissues except for the urinary system had radioactivity concentrations.

The radioactivity curve in the kidneys of the rabbit administered with ^{99m}Tc-(DTPA-ATBA) prepared at pH6 via an ear vein showed that the ^{99m}Tc-complex was rapidly cleared through the kidneys.

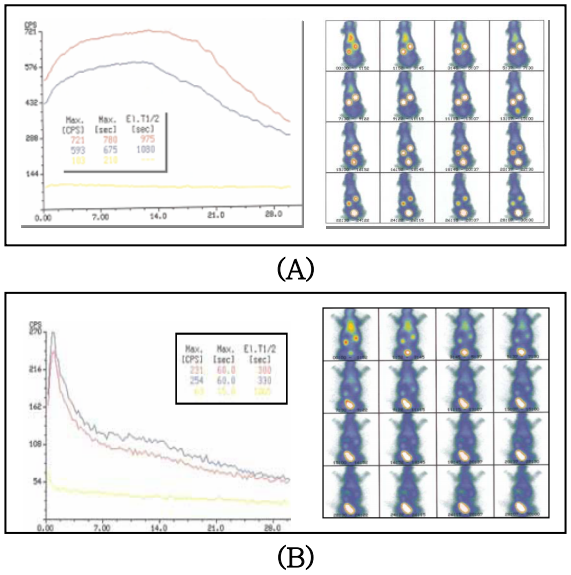


Fig. 2 The time-radioactivity curve of the kidneys and the images of rabbit after an intravenous administration of ^{99m}Tc-(DTPA-ATBA) [A:pH4, B:pH6]

The average of T_{max} and $T_{1/2}$ of the ^{99m}Tc-(DTPA-ATBA) in the kidneys at the different pH of 4 and 6 were showed in the table 1.

	T_{max}(min.)	$T_{1/2}$(min.)
pH 4	11.95	17.13
pH 6	1.00	5.25

Table 1. T_{max} and $T_{1/2}$ of ^{99m}Tc-(DTPA-ATBA) in the kidneys of rabbits

3. Conclusion

^{99m}Tc-(DTPA-ATBA) was revealed a rapid renal clearance, adequate in vivo stability and a low uptake in the vital organs except renal excretive route.

^{99m}Tc-(DTPA-ATBA) can be used as renal function diagnosis and the ligand, DTPA-ATBA, can be applicable for the preparation of the ^{188}Re–complex as a radiation source for the prevention of in-stent restenosis.

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