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Short Research Article

Radiolabelling of thymine with ^{99m}Tc. Preliminary results regarding the stability and biospecificity of [^{99m}Tc]thymine†

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Introduction

This paper reports the radiolabelling of thymine with ^{99m}Tc, as a potential radiopharmaceutical for breast tumor radiodiagnosis in nuclear medicine.[1] We used stannous chloride as a reducing agent in accordance with the requirements of the European Pharmacopeia. Several ratios between thymine and stannous chloride were utilized. In the labelling process, we used a concentration of 1, 2 and 4 mg/ml of thymine (Merck), pH = 5.5, and various stannous chloride concentrations (0.1, 0.25, 0.5 mg/ml) as $SnCl_2 \cdot 2H_2O$ (Merck) in 0.05 N hydrochloric acid. The pH was adjusted with 1 N sodium hydroxide solution to 4.5–5.5, the optimal value for the radiolabelling process. All the preparations of the mixed solutions were effected under an inert gas (nitrogen). After stabilization, the solution obtained was divided into 1 ml portions for lyophilization. The lyophilized samples were radiolabelled by injection of $Na^{99m}TcO_4$ solution (2 ml, 2–10 mCi) eluted from a ^{99}Mo/^{99m}Tc generator. The quality control of the [^{99m}Tc]thymine was monitored by paper and thin-layer chromatography methods. The results show high radiochemical purity (>90%) in accordance with a high radiolabelling yield. The biological properties of the [^{99m}Tc]thymine were evaluated using animal models.

Results and discussion

For evaluation of the radiochemical purity and radiolabelling yield we used the following solvent systems: 0.9% NaCl solution, acetone and isopropyl alcohol/0.1 N hydrochloric acid/water (4:2:4 v/v) for the differentiation between different free and bound ^{99m}Tc species.[2] From Table 1 it can be seen that the radiochemical purity and radiolabelling yield are dependent upon both the mass ratios used and the $Na^{99m}TcO_4$ radioactivity employed in the radiolabelling process.[3,4] The radiochemical purity was calculated by the substraction method. For the radiobiological investigation, we used the samples with composition: thymine:stannous chloride (4:1) mass ratio, labelled with 2.5 mCi of $Na^{99m}TcO_4$. The preliminary results obtained showed that it is possible to obtain [^{99m}Tc]thymine, in high radiochemical purity (90–98%), by employing the optimum composition: thymine:stannous chloride (4:1) mass ratio.

The biospecificity of the uptake of [^{99m}Tc]thymine was evaluated via an animal model using a scintigraphy

Table 1 Radiochemical purity of [^{99m}Tc]thymine complex

Thymine (mg)	Stannous chloride (mg)	$Na^{99m}TcO_4$ radioactivity (mCi)	Radiochemical purity (%)
1	1	5	91.22
1	1	5	89.88
1	0.5	5	90.31
1	0.5	5	92.74
1	0.5	2.5	98.23
1	0.25	5	97.12
1	0.25	5	97.35
2	0.5	8	97.44
2	0.5	2.5	98.15
4	0.5	8	69.54
4	0.5	2.5	68.58

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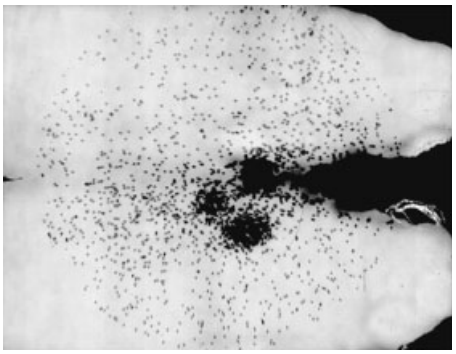

Figure 1 [^{99m}Tc]Thymine uptake by the tumor of the standard female rat (0.8 mCi [^{99m}Tc]thymine in 0.2 ml injected dose).

method. The scintigraphy was carried out within 60 min of the i.v. injection time (Figure 1). The imaging obtained shows the high uptake of [^{99m}Tc]thymine at the tumor after 1 h post-i.v. injection.

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