

Biodistribution and synthesis of ^{99m}Tc -labeled chitosan-transferrin derivative at CT26 colon carcinoma-induced BALB/c mouse

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Purpose: Transferrin (Tf) is a glycoprotein, which transports ferric ion in the body. It is well known that Tf receptor concentration in tumor cells is much higher than that in normal cells. Chitosan is known as a bioactive agents for carriers of DNA, anticancer agents, and radio-labeled molecules. The purpose of this study is to investigate the potential of Tf-conjugated thiolated glycine chitosan(CGGT) for Tc-99m labeled cancer imaging agent. **Methods:** Tf was coupled to the thiol group of thiolated glycine chitosan via maleimidobenzoic acid N-hydroxysuccinimide ester (MBS). Tf-CGGT (0.5 mg) or CGGT (0.5 mg) in water (0.5 ml) was added to Tc-99m solution (50 mCi/0.5 ml) reduced by SnCl_2 . This solution incubated for 30 m, and then determined the radiochemical purity (>93%) by RadioTLC scan. In plasma, Tc-99m CGGT or Tc-99m CGGT-Tf showed the stability of above 90% for 6h. CT26 colon carcinoma cells (1×10^7 cells) were subcutaneously injected into the back of the BALB/c mouse and left for 2 weeks. The biodistribution study with sacrificed mouse at 30, 60, 180 m was performed. **Results:** 97.7% and 93.5% of Tc-99m were labeled to the CGGT and CGGT-Tf at 30 m, respectively. After 60 m, Tc-99m labeling efficiency was 99.4% of CGGT and 95.0% of CGGT-Tf. In the biodistribution study, Tc-99m labeled CGGT was primarily accumulated in the liver(33.3%ID/g), spleen(13.4%ID/g), kidney(17.0%ID/g) and tumor (0.7%ID/g) at 30 m. Tc-99m labeled CGGT-Tf was distributed in the liver (27.9%ID/g), spleen (6.3%ID/g), kidney (12.8%ID/g) and tumor (1.2%ID/g) at 30 m. **Conclusion:** CGGT-Tf was synthesized as a novel Tc-99m labeling agent. The labeling efficiency was high from 30 m after labeling, indicating that CGGT-Tf has a potential of radio-labeled agent. Most of the Tc-99m labeled CGGT-Tf was accumulated in reticuloendothelial systems. Tumor accumulation of Tc-99m labeled CGGT-Tf at CT26 colon carcinoma bearing mouse was twice higher than that of CGGT, indicating that CGGT-Tf has a potential to target and visualize tumor.

Synthesis, biodistribution and imaging of ^{99m}Tc -7-HYNIC-TAXOL

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Purpose: Taxol has been used in the treatment of breast, ovary and lung cancers. To evaluate the feasibility of ^{99m}Tc -7-HYNIC(hydrazino nicotinamide)-taxol as a tumor imaging agent, it was synthesized, and its biodistribution and gamma camera image were obtained in B16-F10 melanoma bearing C57BL6 mice. **Methods:** 7-t-BOC-HYNIC-taxol was synthesized through six steps, and 7-HYNIC-taxol was finally obtained by t-BOC deprotecting from 7-t-BOC-HYNIC-taxol. The product was purified by column chromatography. ^{99m}Tc -7-HYNIC-taxol complex from 7-HYNIC-taxol was prepared by labeling with ^{99m}Tc in the presence of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ and tricine. The biochemical behaviors of the complex such as in vitro stability and lipophilicity, in vitro transchelation were investigated. The biodistribution and in vivo image of ^{99m}Tc -7-HYNIC-taxol were obtained in B16-F10 melanoma bearing C57BL6 mice. After 1, 6 and 24 hr post-injection, the weight and radioactivity of each organ were measured and gamma camera image was obtained. **Results:** The total synthetic yield of 7-HYNIC-taxol was 42.6%. Radiolabeling yield of ^{99m}Tc -HYNIC-taxol was 99.9%. ^{99m}Tc -7-HYNIC-taxol was stable at 37°C for 24 hrs. ^{99m}Tc -7-HYNIC-taxol was slightly more soluble in water than in organic solvent. The binding ability of ^{99m}Tc -7-HYNIC-taxol to serum proteins was 39.9%. In vivo transchelation test, the ^{99m}Tc -7-HYNIC-taxol retained over 86% of radiochemical purity after incubation with DTPA or cysteine. ^{99m}Tc -7-HYNIC-taxol was intravenously administered to C57BL6 mice bearing B16-F10 melanoma at footpad. Tumor/blood ratios were 1.17, 26.0, and 2.87, and tumor/muscle ratios were 12.2, 168, and 15.0 at 1 h, 6 h and 24 h post injection, respectively. The gamma camera image was obtained at 6 h post injection showed selectively localized in tumor. **Conclusion:** ^{99m}Tc -7-HYNIC-taxol showed high stability and was selectively localized in B16-F10 melanoma. These results suggest that ^{99m}Tc -7-HYNIC-taxol can be used as tumor imaging agent.