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

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Purpose: Tranferrin (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 (1×107 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.

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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 99mTc-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. 99mTc-7-HYNIC-taxol complex from 7-HYNIC-taxol was prepared by labeling with 99mTc in the presence of SnCl2·2H2O 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 99mTc-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 99mTc-HYNIC-taxol was 99.9%. 99mTc-7-HYNIC-taxol was stable at 37? for 24 hrs. 99mTc-7-HYNIC-taxol was slightly more soluble in water than in organic solvent. The binding ability of 99mTc-7-HYNIC-taxol to serum proteins was 39.9%. In vivo transchelation test, the 99mTc-7-HYNIC-taxol retained over 86% of radiochemical purity after incubation with DTPA or cysteine. 99mTc-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:** 99mTc-7-HYNIC-taxol showed high stability and was selectively localized in B16-F10 melanoma. These results suggest that 99mTc-7-HYNIC-taxol can be used as tumor imaging agent.