Rhenium-188 방사성 의약품

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Labelling with Rhenium-188

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Abstract

There is considerable interest in ^{188}Re due to its favorable properties as a therapeutic radionuclide. ^{188}Re and ^{99m}Tc act as a matched pair because of their similar chemical properties, and therefore methods of labeling with ^{99m}Tc can be applied to the labeling with ^{188}Re. With appropriately chosen agents as carriers of ^{188}Re, the labeling can be readily carried out using $^{188}ReO_4^-$ in the presence of a reducing agent. ^{188}Re radiopharmaceuticals based on ^{99m}Tc complexes have been synthesized and are currently being studied for clinical use. Some of them are shown to be suitable for therapeutic use and promising for radiotherapy in nuclear medicine. **(Korean J Nucl Med 1999;33:193-5)**

Key Words: Re-188, Tc-99m, Radiopharmaceuticals, Radiotherapy

Labelling with ^{188}Re

Radiopharmaceuticals have been used for the diagnosis and treatment of human diseases, mostly for the diagnostic purposes in nuclear medicine. In recent years, clinical demands on therapeutic radiopharmaceuticals have been increasing, and particularly, complexes labeled with ^{188}Re are drawing much attention due to favorable properties of ^{188}Re. ^{188}Re has a 17-hour half life with a beta energy of 2.12 MeV and 155-keV gamma emissions at 15% abundance which would allow gamma imaging of leakage to other organs. As with ^{99m}Tc, $^{188}ReO_4^-$ obtained in a carrier-free form from the $^{188}W/^{188}Re$ generator is a nonreactive species and thus does not react with any compounds. Therefore, prior reduction of ^{188}Re from the VII state to a lower oxidation state is required, using a reducing agent such as stannous chloride. The resulting reactive species is used for labeling. Re and Tc, which belong to Group VII of the periodic table, have similar chemical properties. In a same vein, Re complexes are also structurally identical to the Tc counterparts, which is supported by crystal structures of the amide thiolate N_2S_2 chelate family indicating identical bond lengths and bond

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angles for Re and Tc complexes.[1] Moreover, chemical characterization of Re complexes can be readily carried out using non-radioactive ^{185}Re complexes, whereas there is no non-radioactive element for Tc. This finding enables one to prepare ^{188}Re radiopharmaceuticals in the same way as the corresponding ^{99m}Tc complexes although labeling with ^{188}Re is more difficult than with ^{99m}Tc.

^{188}Re radiopharmaceuticals

^{188}Re complexes can be used for radiotherapy which allows a desirable high dose of radiation to the site of action. ^{188}Re complexes prepared for this purpose range from simple complexes such as ^{188}Re-HEDP, DMSA, etc. to ^{188}Re-monoclonal antibodies via bifuctional ligands.

^{188}Re-DTPA,[2,3] ^{188}Re-MAG_3 or $^{188}ReO_4^-$ filled in a balloon has been prepared to prevent restenosis after coronary angioplasty and tested for safety in case of balloon rupture using animals. The former two radiopharmaceuticals are preferable because of their rapid excretion via urinary system and currently being used in patients for angioplasty balloon radiotherapy.

^{188}Re-HEDP can be used for bone pain palliation based on bone seeker agents, ^{99m}Tc-diphosphonates. This complex is synthesized in high yield at acidic pH under carrier ($KReO_4$)-added condition. ^{99m}Tc(V)-DMSA has been shown to localize in medullary thyroid carcinoma and head and neck cancer. This result suggests a possible use of the corresponding ^{188}Re complex for tumor therapy. High selectivity for bone metastases in cancer patients demonstrates that ^{188}Re(V)-DMSA may be used for treatments of metastatic bone pain as well as tumor therapy.[4,5]

It has been shown that radiation synovectomy can be an effective treatment of the rheumatoid arthritis. ^{188}Re sulfur colloid and ^{188}Re tin colloid have been prepared as radiation synovectomy agents and showed high labeling efficiency and stability. Particle size can be varied depending on the labeling conditions and the size ranging from 2 to 5 μ m has been shown to be desirable to reduce leakage of radionuclide from the injected site.[6,7] This colloidal ^{188}Re might be further utilized for targeting liver cancer when it is suspended in lipiodol and injected via hepatic artery because this colloid in lipiodol has been shown to be a good hepatic capillary blocking agent.[8]

In addition, ^{188}Re labled sulfur or tin colloid can be used to prepare beta-ray emitting paper for treatment of skin cancer.[9] Monoclonal antibodies labeled with ^{188}Re can be applied to cancer radioimmunotherapy. In most cases, labeling of antibodies is carried out using bifunctional ligands and stannous chloride. Those bifunctional ligands mainly include N_2S_2 and N_3S ligands which easily form complexes with ^{188}Re. Active ester groups of the complexes (^{188}Re-N_2S_2 or ^{188}Re-N_3S) are conjugated with the lysine amino groups of the monoclonal antibodies.

Therapeutic radiopharmaceuticals should accumulate selectively on the target organs while giving minimal radiation doses to surrounding normal tissues. ^{188}Re radiopharmaceuticals are suitable for this purpose and expected to be widely used for radiotherapy in nuclear medicine.

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