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Chemical Control of Biological Activity and Biodistribution of Metal Compounds: Drug Design of Metal Complexes with Biological Activity and Target-Specific Biodistribution

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Abstract:
The development of metallic compounds for the diagnosis and therapy of diseases has been expected to open a new field of medicinal science. These compounds are required to exhibit biological activity and a specific localization to the target tissue. These demands constitute a great challenge on the rational design of metallic compounds and we have proposed two approaches, a pendant approach and an integrated approach in order to achieve this purpose. The pendant approach involves designing a biologically active compound by the attachment of a chelating group for binding the metal ion to a mother compound without the effect on the inherent biospecificity of the mother compound. A typical example of the pendant approach is bifunctional radiopharmaceuticals used for nuclear medical diagnosis and internal radiotherapy. The integrated approach involves designing a metallic compound with a biologically activity and physicochemical properties suitable for target-specific delivery by coordination to a mother compound with metal ion.
This review will describe our recent progress in research on a bifunctional radiopharamceutical labeled with metallic radionuclides, Rhenium-186 for therapy of painful bone metastases as an example of the pendant approach and a lipophilic zinc complex with

protective effect against ischemic neuronal injury as an example of the integrated approach.

Key words: metallic compound, drug design, bifunctional radiopharmaceutical, rhenium-186, bisphosphonates, zinc, neuroprotection.

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