Contrast Agents III: Radiopharmaceuticals—From Diagnostics to Therapeutics

W. Krause, ed.

New York, NY: Springer-Verlag, 2005, 222 pages, $189

The main goal of this book is to provide the reader with the chemical, radiochemical, and biologic knowledge necessary for the development of target-specific radiopharmaceutical compounds. The book consists of 7 chapters of articles devoted almost entirely to radiometal chelates. The first 4 chapters, which focus on the synthesis and characterization of the technetium and rhenium complexes, are followed by 2 chapters on applications specific to molecular imaging and a final chapter on the radiolabeled compounds used in radiotherapy.

Chapter 1 gives an excellent overview of ^{99m}Tc-based imaging agents, followed by a thorough treatment of the ^{99m}Tc-CO complexes. The synthesis and some fundamental properties of these complexes are discussed. The reactions involved in ^{99m}Tc-CO synthesis are critically highlighted, and the versatility and utility of the ^{99m}Tc-CO chemistry in the development of novel radiopharmaceutical compounds are convincingly demonstrated. The chapter concludes with some examples of new central nervous system receptor ligands and of peptides and proteins radiolabeled with ^{99m}Tc-CO complexes.

Chapter 2 reviews the chemistry of technetium and rhenium complexes, focusing on 2 classic heterofunctional phosphine and borate (scorpionate) chelators. Synthetic procedures, reactivity studies, and structural characteristics of these complexes are discussed in detail. The coupling of phosphine and scorpionate chelators to biologically active substances, including those targeting gastrin-releasing peptide receptors and the 5-hydroxytryptamine subclass 1A (5-HT_{1A}) of serotonergic receptors, is described throughout this chapter.

The nitrido complexes of technetium and rhenium are covered in chapter 3. This chapter includes a brief introduction discussing the electronic structure of the Tc≡N bond and coordination geometry, which is helpful in understanding the underlying chemical principles of nitrido ^{99m}Tc/^{188}Re complexes. Examples of the applications of nitrido ^{99m}Tc chemistry for imaging 5-HT_{1A} receptors and for labeling novel DNA binding ligands are provided. Chapter 3 also includes a section on the potential radiotherapy applications of ^{188}Re complexes.

Chapter 4 addresses technetium labeling of small biomolecules with bifunctional coupling agents, in particular 6-hydrazinonicotinamide (HYNIC). Among the subjects covered are practical issues involved in successful radiolabeling, including the stability of the HYNIC-biomolecule conjugates, kit formulations, the selection of coligands, and labeling efficiency. This chapter concludes with a description of various ^{99m}Tc complexes that use HYNIC biomolecules as agents to image thrombi, infection, inflammation, and tumors.

In chapters 5 and 6, the imaging agents used to assess multidrug resistance (MDR) and somatostatin receptors are reviewed. Both classes of imaging agents have already been used clinically in cancer patients. Regarding MDR imaging, ^{99m}Tc-sestamibi and several other ^{99m}Tc complexes that are useful for SPECT are discussed. Radiopharmaceutical compounds used in PET for the analysis of MDR activity, in particular the MDR substrate that forms stable complexes with ^{64}Cu, are briefly covered in chapter 5. Chapter 6 deals with the radiolabeling of somatostatin analogs for PET; this chapter first reviews PET radionuclides suitable for labeling somatostatin and then provides information on somatostatin analogs labeled with gallium, copper, yttrium, and halogen. The radiochemistry and preclinical and clinical studies on these compounds are discussed.

The transition from diagnosis to therapy is discussed at the end of the book, in chapter 7, which describes the ligands of the ^{90}Y-labeled peptide and the nonpeptide integrin $\alpha v\beta 3$ that are used for the treatment of $\alpha v\beta 3$ receptor–positive tumors. This chapter focuses on radiopharmaceutical design, the selection of appropriate radionuclides, and the effect of the chelator on the pharmacokinetics of yttrium-labeled, integrin-targeted radiopharmaceutical compounds.

Overall, this book thoroughly introduces the reader to the current status of radiopharmaceutical agents in diagnosis and therapy and provides sound background information for those interested in radiochemistry. Therefore, the book is a valuable resource for radiochemists and for students, technicians, and researchers seeking additional background information and perspective on the growing field of molecular imaging. The reader should not assume that this book covers all aspects of radiopharmaceutical compounds, as its title suggests. Rather, the book focuses exclusively on the chemistry and applications of radiopharmaceutical compounds that are based on radiometal nuclides.

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