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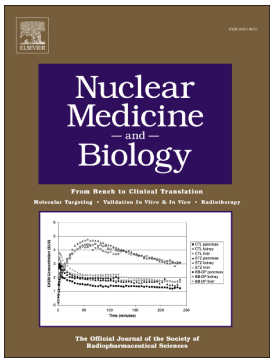

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A Trithiol Bifunctional Chelate for ^{72,77}As: a Matched Pair Theranostic Complex with High *in vivo* Stability

Yutian Feng[1], Anthony J. DeGraffenreid[1,5], Michael D. Phipps[1], Tammy L. Rold[4], Nkemakonam C. Okoye[1], Fabio A. Gallazzi[3], Charles L. Barnes[1], Cathy S. Cutler[2,5], Alan R. Ketring[2], Timothy J. Hoffman[4], and Silvia S. Jurisson[1,2*]

[1]Department of Chemistry, [2]Research Reactor Center (MURR), [3]Molecular Interaction Core, University of Missouri, Columbia, MO 65211, U.S.A. [4]Research Service, Harry S. Truman Memorial Veterans' Hospital, Columbia, MO 65201, U.S.A. [5]Medical Isotope Research and Production Program (MIRP), Collider-Accelerator Department, Brookhaven National Laboratory, PO Box 5000, Building 801, Upton, NY 11973.

Abstract

Introduction: Trithiol chelates are suitable for labeling radioarsenic (^{72}As: 2.49 MeV β^+, 26 h; ^{77}As: 0.683 MeV β^-, 38.8 h) to form potential theranostic radiopharmaceuticals for PET imaging and therapy. To investigate the *in vivo* stability of trithiol chelates complexed with no carrier added (nca) radioarsenic, a bifunctional trithiol chelate was developed, and conjugated to bombesin(7-14)NH_2 as a model peptide.

Methods: A trithiol-BBN(7-14)NH_2 bioconjugate and its arsenic complex were synthesized and characterized. The trithiol-BBN(7-14)NH_2 conjugate was radiolabeled with ^{77}As, its *in vitro* stability assessed, and biodistribution studies were performed in CF-1 normal mice of free [^{77}As]arsenate and ^{77}As-trithiol- BBN(7-14)NH_2.

Results: The trithiol-BBN(7-14)NH_2 conjugate, its precursors and its As-trithiol-BBN(7-14)NH_2 complex were fully characterized. Radiolabeling studies with nca ^{77}As resulted in over 90% radiochemical yield of ^{77}As-trithiol-BBN, which was stable for over 48 h. Biodistribution studies were performed with both free [^{77}As]arsenate and Sep-Pak® purified ^{77}As-trithiol-BBN(7-14)NH_2. Compared to the fast renal clearance of free [^{77}As]arsenate, ^{77}As-trithiol-BBN(7-14)NH_2 demonstrated increased retention with clearance mainly through the hepatobiliary system, consistent with the lipophilicity of the ^{77}As-trithiol-BBN(714)NH_2 complex.

Conclusion: The combined *in vitro* stability of ^{77}As-trithiol-BBN(7-14)NH_2 and the biodistribution results demonstrate its high *in vivo* stability, making the trithiol a promising platform for developing radioarsenic-based theranostic radiopharmaceuticals.