RADIOMETALATTED L-ARGININE DERIVATIVES FOR IMAGING NITRIC OXIDE SYNTHASE *IN VIVO*

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Nitric oxide (NO) is a key mammalian signaling mediator in several physiological processes produced endogenously by conversion of L-arginine to L-citrulline by nitric oxide synthase (NOS). The enzyme presents two constitutively expressed isoforms (nNOS [neuronal NOS] and eNOS [endothelial NOS]) and one inducible isoform (iNOS) [1]. Localized overproduction of NO resulting from NOS upregulation has been linked to cancer and neurological disorders, amongst others [2,3]. Noninvasive imaging of NOS expression *in vivo*, namely by nuclear techniques, holds potential for understanding NO/NOS-related diseases and facilitate the development of novel therapeutic alternatives. Therefore, the use of labeled substrates or inhibitors of NOS with γ- or β^+-emitting radionuclides is a promising approach for *in vivo* imaging of NOS expression [4,5]. We have been involved in the design and biological evaluation of ^{99m}Tc(I)-complexes for probing iNOS [5,6]. Herein, we will describe the synthesis and characterization of novel ^{99m}Tc(I)/Re(I)-complexes containing pendant L-arginine derivatives for NOS recognition. We will also report on the enzymatic activity of iNOS in the presence of those compounds and assess their ability to influence NO biosynthesis in lipopolysaccharide-activated RAW 264.7 macrophages.

Key words: cancer, imaging, nitric oxide synthase, rhenium, technetium-99m

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