ORIGINAL ARTICLE

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5-[^{123}I]Iodo-A-85380: assessment of pharmacological safety, radiation dosimetry and SPECT imaging of brain nicotinic receptors in healthy human subjects

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Recently, 5-[^{123}I]iodo-3-(2(*S*)-azetidinylmethoxy)pyridine ([^{123}I]5IA) was developed as a ligand for imaging the nicotinic acetylcholine receptor (nAChR) in human brain using single photon emission computed tomography (SPECT). In the present study, the toxicity and radiation absorbed dose of [^{123}I]5IA were investigated.

Behavior and physiological parameters were examined in mice and rats after administration of 5IA. There were no changes in these parameters in animals administered 1 μg/kg of 5IA or less, indicating that the no observed effect level (NOEL) of 5IA was 1 μg/kg. [^{123}I]5IA was then administered to healthy human subjects and serial whole-body images were acquired over 24 hr. Initially, high levels of radioactivity were observed in the liver and urinary bladder and moderate levels in the lungs, kidneys, and brain. Whole brain activity at 1 hr was 4.6 ± 0.4% of the injected dose and this value gradually decreased with time. The majority (~75%) of the radioactivity was excreted in urine within 24 hr, and less than 1% remained in all organs tested. The biological half-life of [^{123}I]5IA averaged 7.2 ± 4.0 hr. Based on the biodistribution data, radiation absorbed doses were estimated using MIRDOSE 3.1 software with the dynamic bladder model and the ICRP gastrointestinal (GI) tract model. Consequently, the effective dose equivalent was estimated to be 30 ± 1.4 μSv/MBq, which is an acceptable radiation burden. Having determined the safety of this compound, we performed SPECT imaging in a healthy human subject using 171 MBq of [^{123}I]5IA. SPECT images clearly revealed a cerebral distribution of radioactivity that was consistent with the known distribution of central nAChRs in humans. These results suggest that [^{123}I]5IA is a promising ligand for imaging nAChRs in humans, with an acceptable dosimetry and pharmacological safety at the dose required for adequate SPECT imaging.

Key words: 5-[^{123}I]iodo-3-(2(*S*)-azetidinylmethoxy)pyridine, pharmacological effects, radiation dosimetry, single photon emission computed tomography, nicotinic acetylcholine receptor