Design, Synthesis, ^{99m}Tc Labeling, and Biological Evaluation of a Novel Pyrrolizine Derivative as Potential Anti-Inflammatory Agent

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Abstract—The design and synthesis of ethyl 4-(6-amino-7-cyano-2,3-dihydro-1*H*-pyrrolizine-5-carboxamido)-benzoate (KH16) were discussed, and its structure was determined. The anti-inflammatory activity of a new compound was evaluated using in vitro cyclooxygenase (COX) inhibitory assay. KH16 exhibits higher selectivity to COX-2 than to COX-1 with the selectivity index of 3.46. KH16 was labeled with ^{99m}Tc with the maximum radiochemical yield of ^{99m}Tc-KH16 of 90.5 ± 1.5%. Biodistribution of ^{99m}Tc-KH16 in normal, infected, and inflamed mice was studied. The uptake in inflamed muscle was higher than that in normal muscle throughout the examined time interval. This work is a step ahead in the direction of using pyrrolizine derivatives for site-specific delivery to the inflamed tissue.

Keywords: pyrrolizine, anti-inflammatory drugs, COX, technetium-99m, inflammation, infection

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