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TITLE

Quantitative Whole-Body Autoradiography (QWBA) and Microautoradiography (MARG) in Rats following administration of a Peptide Based Erythropietin Receptor Binder

AUTHORS

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ABSTRACT

The biodistribution of a peptide compound that binds to the erythropoietin (EPO) receptor but has no sequence homology to EPO, was evaluated following a single IV (1, 4, 8, 24, 72, 120, 168, 336, and 672 h) or SC (1, 24, and 168 h) dose of the ^{14}C-labeled agent at 5 mg/kg to male Sprague-Dawley rats using QWBA and MARG. Drug- derived radioactivity was selectively distributed to tissues through 672 h and 168 h post-IV or SC dose, respectively. The highest concentrations of radioactivity found at 1 h post-dose were in the renal cortex and medulla, liver, blood vessels, spleen, and bone marrow. There was a marked difference (2- to 3-fold higher) in tissue concentrations in the red pulp compared to the white pulp in the spleen. In general, relative tissue radioactivity concentration profiles were similar at comparable time points following IV and SC administration. The tissue kinetics reflected a more gradual distribution of radioactivity over time following SC administration compared to IV administration. MARG analysis of selected tissues indicated that in the kidney the radioactivity was localized to the glomeruli and tubules. The finding may reflect excretion of drug-derived radioactivity and/or binding of the radioactive moiety to the renal EPO receptors. The MARG results suggested radioactivity partitioned into the liver, the spleen, the lymph nodes and thymus (extramedullary hematopoietic (EMH) sites). MARG on perfused bone marrow showed a very dense covering of exposed grains, which is likely a function of the high density of EPO receptors in the bone marrow. These data show that a peptide with no sequence homology to EPO localizes selectively to known rodent hematopoietic sites.