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Article

A Novel Manganese Complex Effective as Superoxide Anion Scavenger and Therapeutic Agent against Cell and Tissue Oxidative Injury

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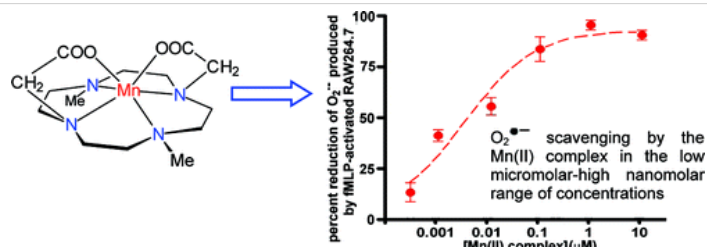
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Abstract



Two cyclic polyamine-polycarboxylate ligands, 1,4,7,10-tetraazacyclododecane-1,7-diacetic acid (H₂L3) and 4,10-dimethyl-1,4,7,10-tetraazacyclododecane-1,7-diacetic acid (H₂L4), and two noncyclic scaffolds, *N*-(2-hydroxyethyl)ethylenediamine-*N,N,N*-triacetic acid (H₃L1) and ethylene-bisglycol-tetracetic acid (H₄L2), form stable complexes with Mn(II) in aqueous solutions. Cyclic voltammograms show that the complexes with the most hydrophobic ligands, [MnL2]²⁻ and [MnL4], are oxidized at higher potential than [MnL1]⁻ and [MnL3]. The pharmacological properties of these molecules were evaluated as superoxide ion scavengers and anti-inflammatory compounds. Among the four complexes, [MnL4] was the most bioactive, being effective in the nanomolar/micromolar range. It abates the levels of key markers of oxidative injury on cultured cells and ameliorates the outcome parameters in animal models of acute and chronic inflammation. [MnL4] toxicity was very low on both cell cultures *in vitro* and mice *in vivo*. Hence, we propose [MnL4] as a novel stable oxygen radical scavenging molecule, active at low doses and with a low toxicity.

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
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