Article

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

Paola Failli†, Daniele Bani‡, Andrea Bencini*§, Miriam Cantore†, Lorenzo Di Cesare Mannelli†, Carla Ghelardini†, Claudia Giorgi§, Massimo Innocenti§, Francesco Rugi§, Alessio Spepi§, Roberto Udisti§ and Barbara Valtancoli§

† Department of Preclinical and Clinical Pharmacology

‡ Department of Anatomy, Histology and Forensic Medicine, Section of Histology

University of Florence, V. le G. Pieraccini 6, Florence, Italy

§ Department of Chemistry, University of Florence, Via della Lastruccia 3, 50019 Sesto Fiorentino, Florence, Italy

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*To whom correspondence should be addressed. Phone: +39-055-4573371, fax: +39-055-4573364, e-mail: andrea.bencini@unifi.it.

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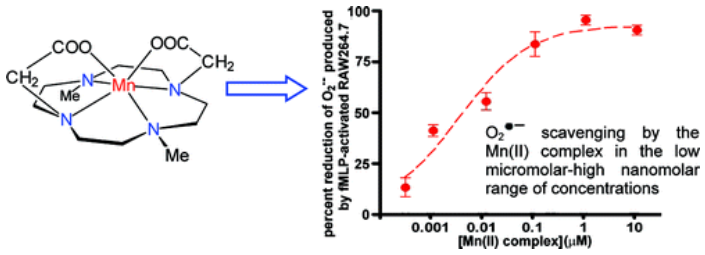
Abstract



Two cyclic polyamine-polycarboxylate ligands, 1,4,7,10-tetraazacyclododecane-1,7-diacetic acid (H_2L3) and 4,10-dimethyl-1,4,7,10-tetraazacyclododecane-1,7-diacetic acid (H_2L4), and two noncyclic scaffolds, *N*-(2-hydroxyethyl)ethylenediamine-*N*,*N*′,*N*′-triacetic acid (H_3L1) and ethylene-bisglycol-tetracetic acid (H_4L2), 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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