ANTIOXIDANTS & REDOX SIGNALING
Volume 14, Number 6, 2011

DOI: 10.1089/ars.2010.3758

Superoxide Dismutase Mimics

Rosalind A. Rosenthal,[1] Susan R. Doctrow,[1] and Wyeth B. Callaway[2]

Dear Editor:

We write to correct some of the misleading descriptions of our research in a Comprehensive Invited Review "Superoxide Dismutase Mimics: Chemistry, Pharmacology, and Therapeutic Potential" by Dr. Ines Batinić-Haberle and colleagues (1). We wish to correct two factual errors and then discuss a matter of opinion.

On page 888, in a section entitled Neutral Porphyrins, our research describing a series of such compounds is cited (2). The review states "Yet, critical analytical data, such as elemental analysis, were again not provided." This statement is incorrect. Analytical data are summarized for all porphyrins in the Materials and Methods section under "Compound Synthesis" (pp. 981–983), with complete elemental analysis and other detailed analytical data provided in the Supplementary Information.

Another line in the same section of the review states "The SOD-like activity has been assayed by NBT assay to avoid the artifact problems with cyt *c* assay, which the authors incorrectly claim were previously observed with MnTBAP." In fact, our article refers to "... interference observed when using MnTBAP analogs," citing Trova *et al.* (3), who describe a series of "MnTBAP analogues," nine of which exhibited artifacts in the cytochrome *c* assay. Specifically, they state "Those porphyrin analogues derived from dipyrromethane 3b and glyoxylate esters 1a-f ... generally interfered with the SOD assay (employing cytochrome *c*)." Our citation, therefore, is by no means an incorrect claim.

While the above comments reflect objective, factual errors in the Batinić-Haberle Review, we wish to add one comment that is more reflective of a difference in opinion. It is further stated in the same paragraph of the review that the compounds we describe have "... no structural features ... [that] would predict them to be good SOD mimics." Our article reports the superoxide dismutase (SOD) and other catalytic activities of our compounds, pointing out that the SOD activity of these Mn porphyrins is, indeed, low when compared with salen–Mn complexes, which we have also described. Unlike Dr. Batinić-Haberle, we believe that SOD activity is not as important as other properties, such as catalase and other reactive oxygen species or reactive nitrogen species scavenging properties, lipophilicity, lack of toxicity, or intracellular stability, in determining biological efficacy (discussed in our article) (2). Our position is further supported by our finding that these neutral Mn porphyrins are potently antiapoptotic in two cellular injury models (2, 4), an important point that Dr. Batinić-Haberle *et al.* fail to mention.

References

1. Batinic-Haberle I, Reboucas JS, and Spasojevic I. Superoxide dismutase mimics: chemistry, pharmacology, and therapeutic potential. *Antioxid Redox Signal* 13: 877–918, 2010.
2. Rosenthal RA, Huffman KD, Fisette LW, Damphousse CA, Callaway WB, Malfroy B, and Doctrow SR. Orally available Mn porphyrins with superoxide dismutase and catalase activities. *J Biol Inorg Chem* 14: 979–991, 2009.
3. Trova MP, Gauuan PJ, Pechulis AD, Bubb SM, Bocckino SB, Crapo JD, and Day BJ. Superoxide dismutase mimetics. Part 2: synthesis and structure-activity relationship of glyoxylate- and glyoxamide-derived metalloporphyrins. *Bioorg Med Chem* 11: 2695–2707, 2003.
4. Vorotnikova E, Rosenthal RA, Tries M, Doctrow SR, and Braunhut SJ. Novel synthetic SOD/catalase mimetics can mitigate capillary endothelial cell apoptosis caused by ionizing radiation. *Radiat Res* 173: 748–759, 2010.

Address correspondence to:
Dr. Susan R. Doctrow
Pulmonary Center
Department of Medicine
Boston University School of Medicine
72 E. Concord St.
Boston, MA 02118

E-mail: sdoctrow@bu.edu

Abbreviation Used

SOD = superoxide dismutase

[1]Pulmonary Center, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts.
[2]Department of Chemistry, University of San Francisco, San Francisco, California.

This article has been cited by:

1. Ivana Ivanovi#-Burmazovi#, Milos# r. Filipovi#Reactivity of manganese superoxide dismutase mimics toward superoxide and nitric oxide **64**, 53-95. [CrossRef]