

This article was downloaded by:

On: 28 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713618290>

Amidothionophosphates: Novel Antioxidant Molecules

Oren Tirosh^a; Yehoshua Katzhendler^b; Yechezkel Barenholz^c; Isaac Ginsburg^d; Ron Kohen^a

^a Department of Pharmacy, The Hebrew University of Jerusalem, Israel ^b Department of Pharmaceutical Chemistry, School of Pharmacy, The Hebrew University of Jerusalem, Israel ^c

Department of Biochemistry, Faculty of Medicine, The Hebrew University of Jerusalem, Israel ^d

Department of Oral Biology, The Hebrew University of Jerusalem, Israel

To cite this Article Tirosh, Oren , Katzhendler, Yehoshua , Barenholz, Yechezkel , Ginsburg, Isaac and Kohen, Ron(1996) 'Amidothionophosphates: Novel Antioxidant Molecules', *Phosphorus, Sulfur, and Silicon and the Related Elements*, 111: 1, 75

To link to this Article: DOI: 10.1080/10426509608054704

URL: <http://dx.doi.org/10.1080/10426509608054704>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

AMIDOTHIONOPHOSPHATES: NOVEL ANTIOXIDANT MOLECULES.

Oren Tirosh[^], Yehoshua Katzhendler^{*}, Yechezkel Barenholz[@], Isaac Ginsburg[^] and
Ron Kohen[^]

[^]Department of Pharmacy, ^{*}Department of Pharmaceutical Chemistry, [^]School of
Pharmacy, [@]Department of Biochemistry, Faculty of Medicine, and the [^]Department
of Oral Biology, The Hebrew University of Jerusalem Israel.

This work describes the synthesis and characterization of a new family of antioxidants. The molecules have the same active group, but different oil-to-water and octanol-to-water partition coefficients due to different substituents. Three new molecules were synthesized based on the chemical structure of the primary amide attached to a thiophosphate group forming an amidothionophosphate. The amidothionophosphate molecules were exposed to the oxidative stress of hydrogen peroxide and sodium hypochlorite, and the chemical changes following the exposure were monitored by ³¹P NMR. The reaction constants with reactive oxygen species such as hydroxyl radical and superoxide radical were also calculated and found to be $1.5 \cdot 10^9 \text{ M}^{-1} \text{ S}^{-1}$ and $8.1 \cdot 10^2 \text{ M}^{-1} \text{ S}^{-1}$, respectively. In order to elucidate the ability of amidothionophosphates to act as antioxidants in protecting lipids and proteins, we examined damage prevention in Bovine serum albumin, egg phosphatidyl choline liposomes and lipid emulsions following oxidative stress. Amidothionophosphate showed unique protection properties in these models. In contrast to other antioxidant molecules (ascorbic acid, cystine, and α -tocopherol) the new group did not have any pro-oxidative effects as measured by oxygen consumption from buffer solutions containing amidothionophosphates and cupric sulfate as a redox-active metal. Amidothionophosphates reduced significantly and in a dose-dependent manner the oxidative burst in human neutrophils as measured by luminol-dependent chemiluminescence, and they also markedly depressed the killing of human fibroblasts by mixtures of glucose oxidase and streptolysin S. The toxicity of these molecules was tested by i.p. injection of up to 1000 mg/kg to white Sabra mice. No mortality was observed 30 days after administration of up to 500 mg/kg.