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# Role of Metallothionein in Free Radical-scavenging and Cytoprotective Activities

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**Key Words**
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**ABSTRACT**

Metallothionein is a low-molecular-weight, cysteine-rich, zinc-binding protein. Increased expression of metallothionein with nuclear localization has been found during development, in certain tumors, and with oxidative stress. Furthermore, metallothionein can protect cells from cytotoxicity and DNA damage. In this study, the antioxidative activity of metallothionein was investigated using 4 *in vitro* models. Metallothionein concentration-dependently (5-20 μM) inhibited non-enzymatic iron-induced lipid peroxidation in rat brain homogenates. Metallothionein (5-50 μM) also scavenged the stable free radical, 1,2-diphenyl-2-picrylhydrazyl (DPPH). In addition, metallothionein also significantly inhibited superoxide anion formation stimulated by formyl-Met-Leu-Phe (FMLP) (100 nM) in neutrophils. Further studies using an electron spin resonance (ESR) method were conducted on the scavenging activity of metallothionein on the free radicals formed. Metallothionein (10 and 20 μM) concentration-dependently reduced the ESR signal intensity of the superoxide anion, the hydroxyl radical, and methyl radical formation. On the other hand, we also found that metallothionein almost completely restored cell viability and promoted cell proliferation in $H_2O_2/Fe^+$ stimulated human umbilical vein endothelial cells. Our results indicate that metallothionein is a potentially effective antioxidant and free radical scavenger as well as a cytoprotectant against oxidative damage. (N. Taipei J. Med. 2001; 3:253-261)

## INTRODUCTION

Metallothionein is a highly conserved low--molecular-weight, thiol-rich protein. Mammalian metallothionein has 61 amino acids, including 20 cysteine residues but no aromatic amino acid, histidine, or leucine.[1] The basal level of metallothionein in biological systems is very low, although it may vary with age and type of tissue. However, this protein is induced to a significantly high level when a system is challenged by heavy metals, starvation, heat, inflammation, or other stress conditions.[2]

Oxygen free radical species are known to be involved in many important biological reactions. Several harmful reactions such as membrane peroxidation, DNA degradation, and destruction of endothelial cells

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