



Review

Copper, oxidative stress, and human health

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Abstract

Copper (Cu), a redox active metal, is an essential nutrient for all species studied to date. During the past decade, there has been increasing interest in the concept that marginal deficits of this element can contribute to the development and progression of a number of disease states including cardiovascular disease and diabetes. Deficits of this nutrient during pregnancy can result in gross structural malformations in the conceptus, and persistent neurological and immunological abnormalities in the offspring. Excessive amounts of Cu in the body can also pose a risk. Acute Cu toxicity can result in a number of pathologies, and in severe cases, death. Chronic Cu toxicity can result in liver disease and severe neurological defects. The concept that elevated ceruloplasmin is a risk factor for certain diseases is discussed. In this paper, we will review recent literature on the potential causes of Cu deficiency and Cu toxicity, and the pathological consequences associated with the above. Finally, we will review some of the potential biochemical lesions that might underlie these pathologies. Given that oxidative stress is a characteristic of Cu deficiency, the role of Cu in the oxidative defense system will receive special attention. The concept that excess Cu may be a precipitating factor in Alzheimer's disease is discussed.

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Abbreviations: A β , amyloid- β ; AD, Alzheimer's disease; AGE, advanced glycosylated end products; ALS, amyotrophic lateral sclerosis; APP, amyloid precursor protein; BH₄, tetrahydrobiopterin; CJD, Creutzfeldt–Jakob disease; eNOS, endothelial nitric oxide synthase; ICC, Indian childhood cirrhosis; ICT,

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idiopathic Cu toxicosis; Mn, manganese; NO, nitric oxide; RDA, Recommended Dietary Allowance; ROS, reactive oxygen species; Se-GPx, selenium-dependent glutathione peroxidase; SOD, superoxide dismutase; TBARs, thiobarbituric acid reactive substances; UL, tolerable upper intake level

Keywords: Cu deficiency; Cu toxicity; Oxidant defense system; Superoxide dismutase; Ceruloplasmin; Metallothionein; Oxidative stress; Oxidative damage; Diabetes; Cardiovascular disease; Alzheimer's disease; Pregnancy; Nitric oxide

Contents

1. Introduction	269
2. Metabolic function and essentiality of copper	270
3. Copper and the oxidant defense system	272
3.1. Superoxide dismutases	272
3.2. Ceruloplasmin	273
3.3. Catalase	273
3.4. Selenium-dependent glutathione peroxidase (Se-GPx)	273
3.5. Glutathione	274
3.6. Metallothionein	274
4. Copper deficiency, reactive oxygen species, and oxidative damage	275
4.1. Oxidant defense genetic knockouts	276
5. Copper, chronic diseases and pregnancy	277
5.1. Diabetes	277
5.2. Cardiovascular disease	279
5.3. Pregnancy and pregnancy outcome	281
6. Copper deficiency and nitric oxide metabolism	281
6.1. Cu deficiency and increased protein nitration	283
7. Copper toxicity	284
7.1. Copper poisoning	284
7.2. Dietary copper toxicity	285
7.3. Wilson's disease	285
7.4. Copper and Alzheimer's disease (AD)	286
Acknowledgements	287
References	287

1. Introduction

The essentiality of copper (Cu) was established in 1928 when it was demonstrated that a deficit of Cu resulted in anemia in rodents (Hart et al., 1928). Cu deficiency is now recognized to be a common problem in many domesticated and wild animals, and marginal Cu deficiency is a problem in some human populations. Conversely, Cu toxicity, typically due to genetic disorders, can also be a significant health

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