

Important Zinc-Selenium Interactions in Humans

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INTRODUCTION

Agronomic Biofortification of Food Crops with Zn and Se

Biofortification of staple food crops with micronutrients by either breeding for higher uptake efficiency or by fertilisation can be an effective strategy to address widespread dietary deficiencies in human populations (Graham et al. 2001).

Zinc and Se deficiencies in soils and humans are common in large parts of Africa, China and Turkey. Mounting evidence of important beneficial interactions between Zn and Se underscores the need to provide both micronutrients together under conditions of concurrent deficiency (Lyons et al. 2004). Following is a brief review of studies that have found interactions between Zn and Se in humans.

BRIEF REVIEW

Human Studies Showing Zn and Se Interaction

A role for Se in regulating, or normalising, the levels of other micronutrients at key sites in the body has been suggested by a clinical trial in Serbia, a low-Se country. The participants were moderately deficient at baseline in Se, Zn, Fe and copper (Cu), while manganese (Mn) status was higher than normal. Those individuals who consumed Se-biofortified wheat (which increased daily Se intake by 18µg, or 58%) during the trial increased plasma Se concentration by 52% after six weeks, and also had increased concentrations of Zn, Fe and Cu in erythrocytes, while Mn concentration declined in both plasma and erythrocytes (Djujic et al. 2001).

At the molecular level, several studies indicate that, although “biochemical” Zn is redox inert (unlike Fe and Cu), there is a link between cellular Zn and redox state. Zn binds to sulphhydryl groups in proteins, thus stabilising protein conformation. But oxidation causes disulphydryl formation which leads to membrane leakiness (Bettger & O’Dell. 1981). The storage protein metallothionein (MT) coupled with thionein (T) has the function of preserving Zn and controlling the concentration of available Zn in the cell. The low redox potential of sulphur (S) donor atoms in Zn/S cluster bonds in thiol groups of MT allows oxidation by mild cellular oxidants, including several Se compounds, with resultant release of Zn. On the other hand, antioxidant Se compounds act to preserve Zn binding, thus regulating Zn delivery from MT to Zn enzymes (Maret et al. 2000). Hence cellular redox state determines Zn distribution by promoting Zn release under oxidising conditions, and promoting Zn binding under reducing conditions. This shows an interaction between Se and Zn/S centres, and the author suggests that a consequence of Se deficiency may be reduced Zn status (Maret. 2000).

Further evidence for the involvement of Se in Zn homeostasis is provided by the studies of Blessing et al. (2004). These authors compared the ability of various Se compounds with the strong oxidant hydrogen peroxide, the cellular oxidant oxidised glutathione (GSSG) and the antioxidant reduced glutathione (GSH) to release Zn from the Zn finger domain of a DNA repair protein. Reducible Se compounds (with an oxidation state of -1 and above), including selenocyanate, selenocystine and phenyl selenilic acid have an important role in modulating Zn repair-DNA interactions, releasing between 22% and 50% of Zn, compared to 100% for H₂O₂ and zero for pure water. The study also suggests that reducible Se compounds are able to attack Zn-S bonds under cellular conditions, where GSH/GSSG ratios between 1 and 3 for

the endoplasmic reticulum and between 40 and 100 for the overall cell have been reported (Hwang et al. 1992). The authors conclude that, as redox reactions are important for the regulation of Zn finger proteins, an imbalance in Se compounds as important mediators of cellular redox reactions, resulting from either Se deficiency or excess, may increase DNA damage (Blessing et al. 2004). Moreover, a feedback mechanism is likely to be involved, as Zn has been found to up-regulate gene expression of the antioxidant selenoenzyme glutathione peroxidase (Reid and Tervit 1999).

Zn-Se interaction is also evident at transcriptional level. The tRNA^{Sec} gene product is involved in the biosynthesis and co-translational insertion of selenocysteine into selenoproteins. Enhanced transcription is afforded by a Zn finger activator, a 600-amino acid protein with seven Zn fingers comprising the DNA-binding domain (Hubert et al. 1996).

CONCLUSIONS

Important Zn-Se interactions are evident in humans from the molecular level to the whole organism. Especially intriguing is the effect of different Se compounds on release of Zn from thiols, including those within the Zn-preserving metallothionein/thionein couple and Zn-containing DNA repair proteins. Feedback mechanisms are likely to be involved, but our knowledge of these is limited at this stage. Further research is needed on the effects of Zn deficiency on the forms and activity of Se compounds and *vice versa*. These studies highlight the need to consider micronutrient synergies, especially in populations with concurrent deficiencies, in order to maximise the benefits of biofortification programs.

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