ALBION®
HUMAN NUTRITION

RESEARCH NOTES

A COMPILATION OF VITAL RESEARCH UPDATES ON HUMAN NUTRITION

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# Not So Secondary Functions

Minerals and trace minerals are all important for the health of all living things. The body can not make its own minerals. They must be ingested one way or another. Each mineral has a variety of functions in the human body. Some like magnesium have several hundred functions via its roles in so many different enzyme systems. Others, like molybdenum are more limited in their number of functions. Often when the various minerals are discussed, however, only the most obvious functions for the mineral being discussed are talked about. Zinc and the immune system, or selenium and its antioxidant impact are examples of this point. However, as mentioned most minerals have multiple functions, and often a mineral has functional effects that although not commonly talked about, are very important to maintenance of a healthy body.

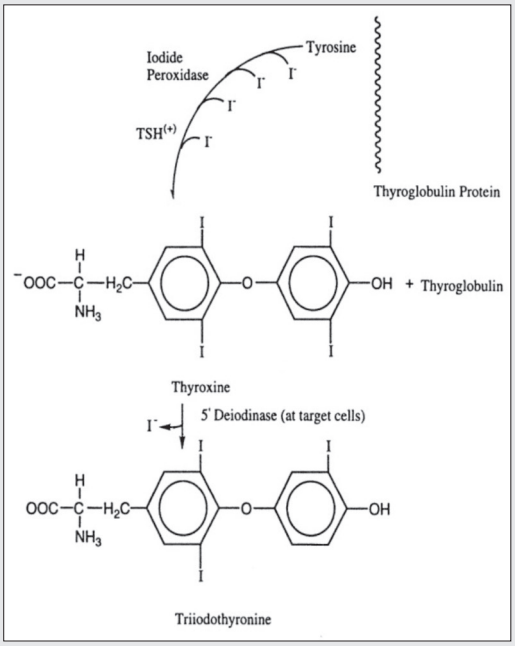
In this issue of Albion's® Research Notes, the "secondary functions" of the following minerals are going to be reviewed: selenium, manganese, zinc, and copper. Most commonly, selenium is known for antioxidant activities in its role with glutathione, and manganese is referred to for its role as a free radical fighter, Manganese SOD, or as a catalyst in the formation of cartilage tissue. Zinc is an important immune system contributor, while copper is looked at for its role in antioxidant activities, often associated with aiding in inflammatory problems, like arthritis. However, as mentioned earlier, minerals have multiple functions that help maintain a healthy body.

## *Secondary Functions*

### Selenium

Selenium is a cofactor for enzymes and proteins of vital importance in antioxidant defense. Additionally selenium is involved with the maintenance of proper thyroid function. There is a group of selenocysteine enzymes known as thyroxine deiodinases. The thyroxine deiodinase 2 (known at 5′ deiodinase) is responsible for the conversion of the prothormone thyroxine T4 into the active hormone triiodothyronine T3 in the thyroid (see Fig. 1). The thyroxine deiodinase 1 inactivates thyroxin in the liver and kidney, thus it insures that this hormonal activity does not accumulate unchecked. Changes in thyroid function can affect mood, behavior, and cognitive function. Given the importance of selenium to proper thyroid function, selenium status can play a role in helping people suffering from the depressed mood associated with hypothyroidism [Med Hypotheses. 2001;57 (4):480-3]. There have been found statistically significant correlations among the indices of selenium status and the indices of thyroid hormone metabolism and function.

*Figure 1.* Schematic representation of thyroid hormone synthesis. The figure below depicts selenium's role via 5' deiodinase.

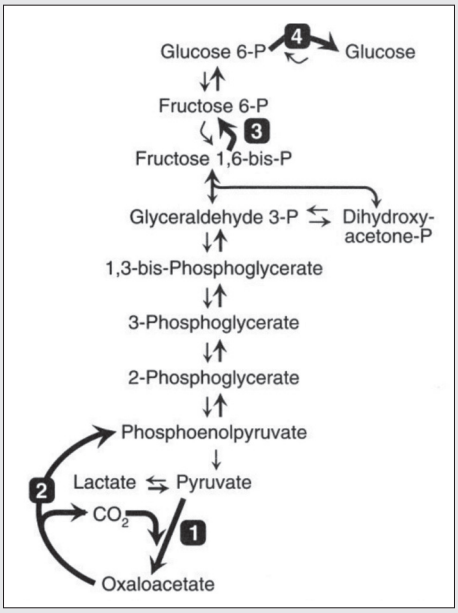



### Manganese

Manganese is known to play a key role in free radical control via its involvement in the Manganese SOD enzyme, and it is required by the glycosyl transferases for participation in the formation of cartilage and other connective tissues. What about its role in glucose and carbohydrate metabolism? Dr. Deborah L. Baly, et al. did several animal studies concerning man-

ganese and its role in this area. Dr. Baly's studies found that manganese deficiency lead to altered carbohydrate metabolism at the level of pancreatic insulin synthesis and gluconeogenesis. Further studies by M.L.White have recognized that the insulin receptor was a hormone dependent kinase that can be stimulated by Mg and Mn, and that manganese activates the insulin receptor protein kinase in vitro via an effect on Mg ATP. M. Ueda, et al., demonstrated that manganese can enhance extracellular binding of insulin to its receptor, facilitates the physiological actions of insulin and mimics the action of the hormone. Manganese deficiency was seen to result in a decrease in the number of glucose transporters in adipose tissue. Baly, et al also have observed that manganese deficient animals had a seven fold lower proinsulin mRNA, resulting in a decreased insulinogenesis. However, it is the actions of the manganese metalloenzyme pyruvate carboxylase and the phosphoeneolpyruvate carboxykinase, a manganese-activated enzyme in the initiation of gluconeogenesis that may be the most key role of manganese in glucose homeostasis (see Fig. 2). Cellular manganese concentration is a key factor in the regulation of carbohydrate metabolism, and plays a role in gluconeogenesis as well.

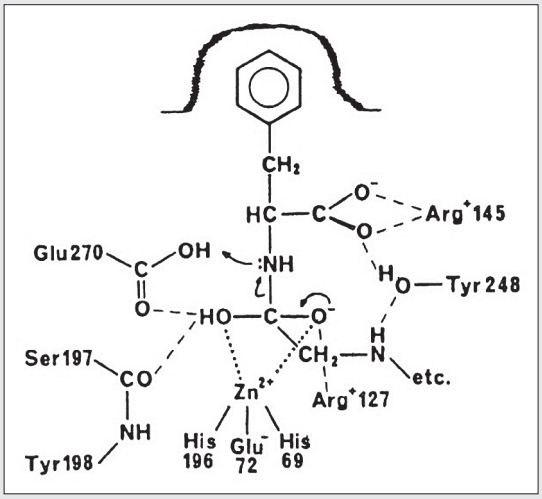
*Figure 2.* Gluconeogenesis
1 = Pyruvate carboxylase
2 = PEP-carboxykinase




## Zinc

Zinc is without question the most talked about of all the immune supportive nutrients, and its role in healing and dermal health is also well known. In addition, it plays an important role in food digestion and absorption. Zinc is an essential cofactor for carbonic anhydrases, proteases, phosphatases and other enzymes involved in the digestion and absorption of food. Carbonic anhydrases work in the production of gastric acid. The carboxypeptidases, which are stabilized by zinc, are zinc dependent digestive enzymes from the pancreas (see Fig. 3). Several peptidases of the intestinal brush border are zinc enzymes, including leucine aminopeptidase, membrane alanine aminopeptidase, glutamyl aminopeptidase, membrane dipeptidase, and a few others. Another brush border zinc enzyme is a form of carboxypeptidase that is needed to cleave off gamma-glutamyl residues from dietary folate prior to absorption. An alkaline phosphatase that requires both zinc and magnesium works at the intestinal brush border to digest complex forms of thiamine, riboflavin and pantothenate. Zinc deficiency is known to result in the impairment in the ability to absorb water and electrolytes, and is a trigger for diarrhea. The gastrointestinal tract may be the first target areas where zinc insufficiency is manifested.

*Figure 3.* Zinc's hold on oxygen in stabilizing carboxypeptidases




## Copper

Copper is essential to antioxidant defenses, brain function, collagen synthesis, and it plays a key role in energy metabolism. The role that copper plays in energy metabolism is sometimes overlooked. In the inner mitochondrial membrane, cytochrome c oxidase catalizes the rate-limiting terminal step of oxidative phosphorylation (see Fig. 4). The copper, in subunit II of this complex, transfers the electrons from cytochrome c to the copper and iron containing center of the catalytic subunit 1. A vectoral Bohr mechanism (conformation shift due to oxygenation change) moves reduced protons from the inner aqueous space through the mitochondrial membrane and the heme-copper oxidases then release them into the

external space [ Papa S., et al, Biochimie, 1998 Oct;80(10):821-36]. This proton translocation builds up a proton gradient or pump across the inner mitochondrial membrane that drives the synthesis of the energy dynamo, ATP .

## *Discussion*

All four of these trace minerals play very important roles outside of what has been their most popularly talked about benefits. In fact all of them are also key players in the body's antioxidant defense systems, as well. Albion produces a Selenium Glycinate Complex, Manganese Glycinate Chelate, a Zinc Glycinate and Zinc Arginate Chelate, as well as a Copper Glycinate Chelate. All of which have been the subject of clinical studies that demonstrate their good bioavailability and safety. In addition, research on these Albion mineral forms have generated some additional findings as to their biological impact.

Studies at Ohio State University under the direction of Dr. Robert DiSilvestro have shown that Albion's Selenium Glycinate Complex, at a dose of 200mcg/day given over the course of 5 weeks to healthy men led to an increase in plasma and erythrocyte glutathione peroxidase, and led to a decrease in plasma PSA levels.

A study by C Davis and JL Greger has shown that the supplementation of Albion's Manganese Glycinate Chelate will improve MnSOD activity and serum manganese concentrations with no changes in urinary manganese excretion or indices of iron status, even when taken along with an iron supplement. This was a significant finding, given that iron supplementation was known to cause a depression in MnSOD, serum manganese, as well as the retention of manganese.

Research conducted on Albion's Zinc Glycinate Chelate and Zinc Arginate Chelate has demonstrated that these two chelates have a higher affinity to the male reproductive system than inorganic forms of zinc. This implies that the Albion zinc forms can have a greater impact on the nutritional health of the prostate and testicular functions of the male. Other studies have shown that the Zinc Glycinate Chelate has vastly superior bioavailability when compared to the popular zinc gluconate (Maurette, et al).

Studies by Dr. Robert DiSilvestro of Ohio State University have shown that Albion's Copper Glycinate Chelate at a dose as low as 2mg per day was able to significantly elevate the CuZn SOD activity in arthritics. Further studies have demonstrated that the use of Copper Glycinate Chelate can significantly elevate Ceruloplasmin, Diamone Oxidase, and CuZn SOD activity, indicating its ability to have a positive impact on all the physiological effects of copper.

Albion's Selenium Glycinate Complex, Manganese Glycinate Chelate, Zinc Glycinate and Arginate Chelate, and Copper Glycinate Chelate have all been shown to be effective and safe forms of mineral supplementation.

*Figure 4*. Oxidative Phosphorylation ATP Generation
Copper involved at Cytochrome C and subunit II