ALBION®
HUMAN NUTRITION

RESEARCH NOTES

A COMPILATION OF VITAL RESEARCH UPDATES ON HUMAN NUTRITION

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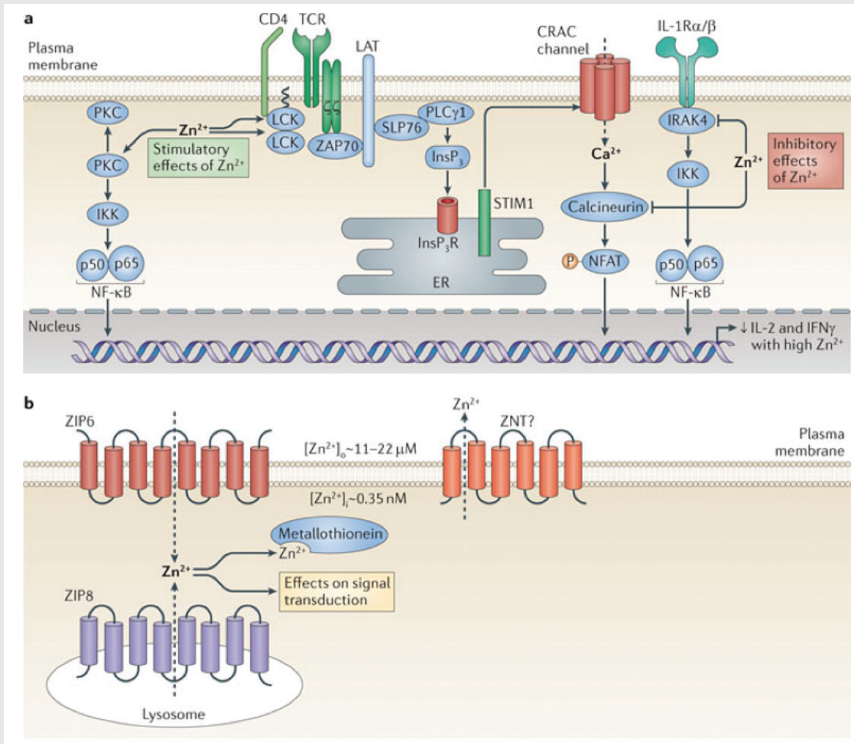
Zinc and Aging

The importance of zinc to body performance and health cannot be overstated. According to Prasad, A.S. [J Trace Elem Med Biol 2014;28(4):357-363], we know of >300 enzymes and >1000 transcription factors that need zinc for their activities. In the case of enzymes, zinc may act as a catalyst or cofactor, while in others for structural stabilization. Zinc is key to the metallo-proteins known as transcription factors, many of these contain what is referred to as zinc fingers (Haase & Rink, Immun&Ageing 2009,6:9). These zinc metalloenzymes play essential roles in a variety of aspects in cellular metabolism, including DNA replication, repair, and transcription. Zinc is involved in cellular proliferation and differentiation. Zinc balance is key in signal transductions, which are responsible for a variety of physiological functions. The diagram (Figure 1.) is an example of a zinc signal transduction. In this instance, Zn+2 ions can activate or inhibit signal transduction in T-cells. Zn+2 mediates the recruitment of the SRC family kinase. SRC family kinase play important roles in selected cellular signaling pathways. Zinc is also involved in the regulation of normal apoptosis, which is the natural cycle of programmed cell death. Too much apoptosis results in atrophy, while too little can lead to things like cancer. Despite the importance of zinc, its stores in the body are quite limited, and can be easily depleted due to high demands as seen in inflammatory conditions and infections.

The immune system requires a continuous supply of zinc for the on-going production and differentiation of the immune cells (Immun&Ageing 2009,6:9). Unfortunately, the incidence of zinc deficiency has not drawn enough attention. According to a review on the subject by J. Nriagu (2007 Elsevier B.V.), zinc deficiency has grown into a nutritional problem worldwide, pandemic in both developed and developing countries. There are two categories for the causes of zinc deficiency: nutritional or conditional. Nutritional causes result from consumption of foods with either low zinc or unavailable forms of zinc, as seen in people who have a high phytate diet. Conditional causes of zinc deficiency are often disease related, stemming from problems like Crohn's Disease and cystic fibrosis. Diseases of genetic malfunction, such as Down's Syndrome and sickle cell disease result in poor zinc absoprtion. Some conditional causes come from excessive loss of zinc, as seen in renal diseases and diabetes. The increased need for zinc, in pregnancy, lactation, stress, and periods of rapid growth are other examples of conditional cause. According to the National Institute of Health Office of Dietary Supplements (on-line zinc review), zinc deficiency can lead to " growth retardation, impaired immune function, and loss of appetite. More severe deficiency has been seen to result in hair loss, diarrhea, delayed sexual maturation, impotence, hypogonadism in males, as well as eye and skin lesions. Weight loss, delayed healing of wounds,

Figure 1.



Nature Reviews/Immunology Vol.5, 2005.

taste abnormalities, and mental lethargy can occur. Many of these symptoms are non-specific and often associated with other health conditions".

Zinc: the Immune System and inflammation

The immune system is a complex group of body components involved in protecting against pathogens, toxins, and other potential body invaders. The immune system is divided into two types of immunity: adaptive and innate. The innate immune system is comprised of components that are always there protecting against microbes at a potential site of infection. It consists of things like skin and other epithelial barriers, phagocytic leukocytes, special lymphocytes called natural killer cells, plasma proteins, and dendritic cells. The adaptive immune systems take over when pathogens are able to overpower the innate system. This adaptive immune system works against invading microbes, by creating methods of terminating or eliminating them – through either humoral or cell mediated immunity. Humoral immunity uses B lymphocytes to make antibodies against microbes, while cell mediated immunity uses T lymphocytes.

According to Bonaventura P, et al (Autoimmun Rev 2014 Nov.24), Zinc deficiency affects cells involved in both innate and adaptive immunity at the survival, proliferation and maturation levels. These cells include monocytes, polymorphonuclear-, natural killer-, T-, and B-cells. T cell functions and the balance between the different T helper cell subsets are particularly susceptible to changes in zinc status. Acute zinc deficiency leads to a decrease in the innate and adaptive immunity, while chronic deficiency increases inflammation. In chronic deficiency, the production of pro-inflammatory cytokines increases, influencing a large number of inflammatory diseases.

Oxidative stress is an important contributing factor for many chronic diseases attributed to aging, such as atherosclerosis and related cardiac disorders, cancers, neurodegeneration, declining cognitive function, immunologic disorders, and the aging process itself (Prasad A., Frontiers in Nutrition, 2014, vol. 1 No. 14). The role of zinc deficiency in the oxidative stress leading to these diseases of inflammation is well-documented. As many as 40% of elderly Americans and 2 billion people globally have diets that are deficient in zinc. People over the age of 55 are the fastest growing segment of the United States' population. This will become a larger problem as time goes on.

Below is an author abstract has that helped shed additional light on age related zinc deficiency and the increased inflammatory response.

C.P.Wong, K Magnuson, E. Ho

JNB Jan.2012 Vol.24, Issue 1 pages 353-359

Aging is a complex process associated with physiological changes in numerous organ systems. In particular, aging of the immune system is characterized by progressive dysregulation of immune responses, resulting in increased susceptibility to infectious diseases, impaired vaccination efficacy and systemic low-grade inflammation. Increasing evidence suggest that intracellular zinc homeostasis, regulated by transporter expression, is critically involved in the signaling and activation of immune cells. We hypothesize that epigenetic alterations and nutritional deficits associated with aging may lead to zinc transporter dysregulation, resulting in decreases in cellular zinc levels and enhanced inflammation with age. The goal of this study was to examine the contribution of age-related zinc deficiency and zinc transporter dysregulation on the inflammatory response in immune cells. The effects of zinc deficiency and age on the induction of inflammatory responses were determined using in vitro cell culture system and an aged mouse model. We showed that zinc deficiency, particularly the reduction in intracellular zinc in immune cells, was associated with increased inflammation and age. Furthermore, reduced Zip 6 expression enhanced pro-inflammatory response, and age specific Zip 6 dysregulation correlated with an increase in Zip 6 promoter methylation. Furthermore, restoring zinc status via dietary supplementation reduced age-associated inflammation. Our data suggested that age-related epigenetic dysregulation in zinc transporter expression may influence cellular zinc levels and contribute to increased susceptibility to inflammation with age.

In the Prasad article is a review of a clinical study that he and co-researchers had published (Am J Clin Nutr 2007 V. 85:837-844). The study was a randomized, placebo controlled trial on the efficacy of zinc with respect to infections and the effect on ex

Table 1. Effect of zinc and placebo supplementation on clinical variables.

Variables	Percentage of subjects affected in 1 year	
	Zinc Group (n=24)	Placebo Group (n=25)
Infection	29	88
Upper respiratory Tract Infection	12	24
Tonsilitis	0	8
Common Cold	16	40
Cold sores	0	12
Flu	0	12
Fever	0	20

(Each person could appear in more than one sub-category of infection)

vivo generated inflammatory cytokines and plasma oxidative stress markers. The study included 50 healthy adults of both sexes and all ethnic groups, ages 55-87, living in a senior citizen center. The supplementation was 45mg of elemental zinc daily, as zinc gluconate. The study measured changes in the different markers of oxidative stress and inflammatory cytokines. The zinc supplemented group exhibited lowered levels of these indicators of stress on the immune system, which included increased zinc related antioxidant power, as compared to the placebo group. In Table 1, the improvements resulting from zinc supplementation is directly reflected in the lower infectious disease incidence seen in the zinc group.

It is clear that zinc deficiency increases with age, and that this decline in zinc status is one of the causes of cell-mediated immune dysfunction, increased oxidative stress, and increased generation of inflammatory cytokines. The neurodegenerative changes that are associated with aging and zinc status are a result of chronic inflammation and oxidative stress. Many pathological changes associated with aging and aging-related disorders have been attributed in part to an increased unregulated production of reactive oxygen species (ROS) in the brain. Zinc has been shown to be a key component of the immune system that is involved in detoxification of ROS, helping to decrease oxidative stress. The complexity of mechanisms through which zinc imparts its action as an antioxidant and anti-inflammatory is theorized by Ananda Prasad and replicated in Figure 2.

As seen in the research presented, the supplementation of zinc can help fight against the many factors associated with chronic degenerative diseases associated with oxidative stress and pro-inflammatory substances, like plasma cytokines. Zinc, in the Prasad study, at a dosage of 45mg of elemental per day had a very positive impact on these factors.

Choose the Right Form of Zinc – it's a Key Mineral

Albion's Zinc Bisglycinate Chelate has been compared in two separate clinical trials to zinc gluconate. The first study (Int J Vitamin Nutr Res., 2007; 77 (4): 243-8) compared the oral bioavailability of Zinc Bisglycinate to zinc gluconate. It was a randomized, crossover deign at an elemental zinc dosage of 15mg/day. The study findings showed that the Zinc Bisglycinate Chelate was safe and well tolerated, and that the bisglycinate form was significantly higher in bioavailability (+43.4%) than the gluconate form. A subsequent clinical trial, DiSilvestro R.A., et al (Biol Trace Elem Res., published on line April 17, 2015), compared a moderately high dose (60mg/day) of zinc as Bisglycinate Chelate to zinc gluconate, following a double blind, placebo controlled protocol. The data gathered showed that the Zinc Bisglycinate Chelate group had a significantly increased plasma zinc, while the zinc gluconate and placebo groups showed no change in plasma zinc. Zinc Bisglycinate Chelate had superior bioavailability to the gluconate form, while not negatively impacting the subjects' copper status.

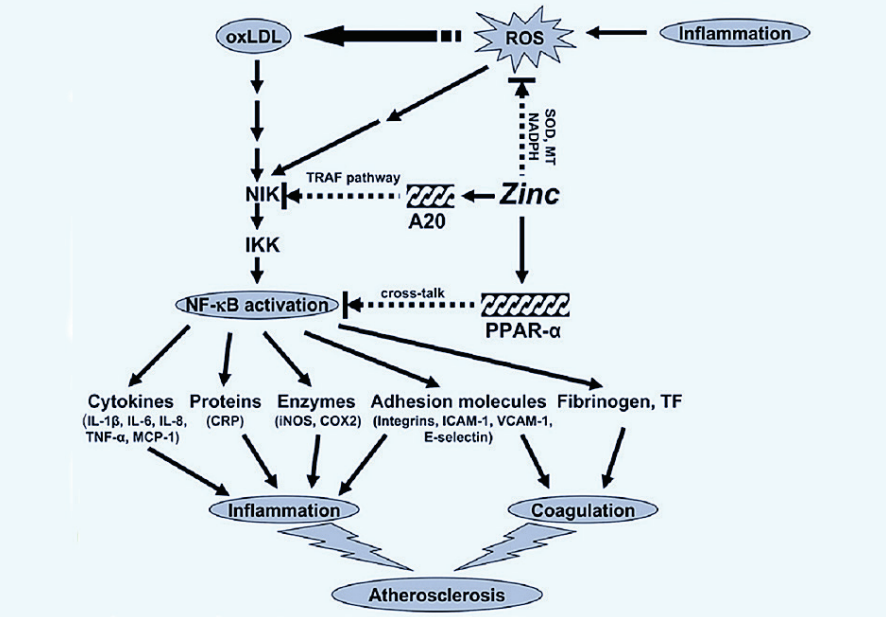
Given the superior bioavailability for Zinc Bisglycinate Chelate to zinc gluconate, it is clearly the better choice for supplementation. In addition the studies have shown that the Bisglycinate Chelate form is safe, well tolerated, and does not negatively impact copper status.

Knowing the high rate of zinc deficiency seen as people age, and the chronic degenerative disorders associated with zinc deficiency, it has been suggested that zinc supplementation might be a good idea, especially as people age. Neurodegeneration is a very critical aspect of zinc deficiency and is a major contributor to a decline in cognitive function.

For the best choice of zinc to supplement, Albion's Zinc Bisglycinate Chelate is that choice!

It is also available in a Taste Free form.

Figure 2. In this particular diagram, the signaling pathway for zinc in the prevention of atherosclerosis in monocytes/macrophages and endothelial cells is theorized. This same pathway is the same for zinc in all chronic diseases associated with oxidative stress and plasma inflammatory cytokines.



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