Zinc: Essential Nutrient for Cellular Metabolism, Immune Function, Reproductive Health & Healthy Aging

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Discussion

Zinc, a non-toxic, biologically-essential trace mineral, is vital for almost all physiological processes. The only metal that is a coenzyme to all classes of enzymes, zinc is a key component of over 300 metalloenzymes. Zinc is essential for over 2000 transcription factors which are involved with gene transcription and regulation of lipid, protein, and nucleic acid metabolism.[1-7] About 10% of the human genome encodes for proteins that can bind zinc.[8] Necessary to maintain the structural integrity of DNA, zinc also plays a role in cellular metabolism, immune function, wound healing, and acts as a messenger in signal transduction. Zinc is vital for growth, reproduction, and reproductive health.[1-8]

The human body contains around two to three grams of zinc, most of which is bound to proteins.[8] Zinc is found in many tissues, especially in the kidneys, liver, brain, muscles, and bones. It is most highly concentrated in prostate tissues and in parts of the eyes. About half the total body zinc is contained in the bones and about 6% in the skin.[2,3]

DIETARY ZINC

Zinc is abundant in red meat and oysters and is also found in eggs, fish, nuts, and dairy products. While cereals and legumes contain moderate amounts of zinc, absorption is often hindered due to their phytate, calcium, and phosphate content. Vegetables contain low amounts of zinc.[2,3,9,10] The RDA (recommended daily allowance) for men is 11mg/day and for women 8mg/day (for adults.).[10]

ZINC NUTRITIONAL STATUS

Zinc, essential for humans, animals, and plants, is deficient in soils worldwide for multiple reasons. This is a contributing factor to inadequate zinc intake by humans.[9] Zinc deficiency is especially common throughout the developing world, where it is estimated to effect about 2 billion people.[2,6,10-12] In developing countries where the diet consists mostly of cereal proteins with high phytates, patients are found to have lower zinc and iron availability, which often expresses as multiple symptoms including iron deficiency anemia, growth retardation, hypogonadism, hepato-splenomegaly, rough, dry skin, and high occurrence of immune dysfunction and infections.[13] The main signs of severe zinc deficiency include retarded growth, hypogonadism in males, cell-mediated immune dysfunctions, and cognitive impairment.[10] Zinc deficiency is also characterized by skin lesions, impaired wound healing, anemia, anorexia, and impaired visual function.[1,8,12]

Because of the far-reaching influence of zinc, even mild zinc deficiency is deleterious to numerous biochemical and immunological functions.[11] It is estimated that about 10% of the population in the United States is not getting adequate dietary zinc.[7]

Zinc is classified as a type 2 nutrient – one that is required for general metabolism (protein and magnesium are also type 2 nutrients). Type 1 nutrients (such as vitamin A, folate, copper, iron) are required for one or more specific functions. Because zinc influences so many biochemical functions (rather than just one or two specific ones), scientists have not identified reliable biomarkers for zinc nutritional status or deficiency.[14]

Therapeutic Actions of Zinc:

- anti-inflammatory
- antioxidant
- messenger in signal transduction
- influences gene expression
- coenzyme to all classes of enzymes
- component of over 300 metalloenzymes
- influences intracellular ion homeostasis

Plasma zinc concentrations decline with moderate deficiency but are also found to decrease with specific conditions including infection, trauma, stress, steroid use, and even after a meal. This is partly caused by the metabolic movement of zinc from plasma to the tissues and makes it difficult to accurately determine zinc status from plasma levels. Research suggests that measures of metallothionein or of cellular zinc transporters (see section below) may give a more accurate picture of an individual's zinc status.[14]

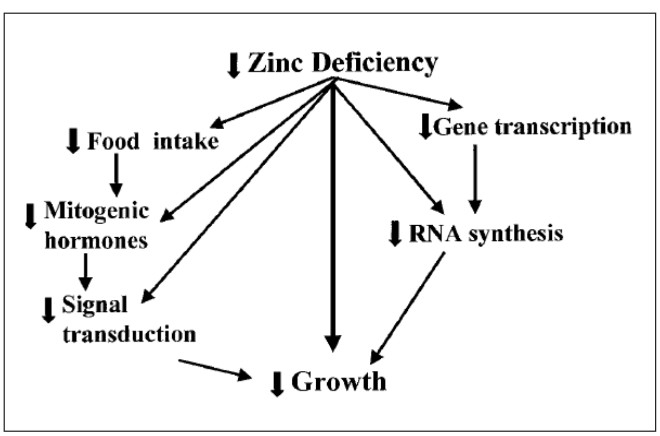
Minerals have complex interrelationships in the human body and an excess or deficiency in one mineral can have an adverse influence on mineral homeostasis. Studies find that diets high in calcium can reduce zinc absorption and levels.[15] While zinc is non-toxic, excess zinc consumption (over 40mg/day for adults) can upset physiological mineral homeostasis and contribute to copper deficiency.[10,15] Zinc also influences metabolism of vitamin A, including absorption, transport, and utilization through several pathways.[16]

HORMONE AND PROSTATE HEALTH

Zinc is essential in the formation of hormone receptor proteins and for nuclear binding of androgen receptors. Zinc influences synthesis and secretion of hormones including LH (luteinizing hormone) and FSH (follicle-stimulating hormone). It is a key factor in gonadal differentiation, testicular growth, and many other aspects of male reproductive health. Hypogonadism is indicative of significant zinc deficiency in animals and humans.[2,4,17,18]

Zinc is an essential element in prostatic fluid and high amounts of zinc are secreted in the prostatic fluid. Zinc plays a key role in prostate health, influencing immunologicial, infectious, and neoplastic developments.[19-21] Total zinc concentration in the prostate is about ten times that in other soft tissues. A significant decrease in tissue zinc levels is seen in prostate disease.[20]

Studies find that zinc concentrations in malignant prostate tissues are only 10% to 25% of those in normal prostate tissue.[22] This suggests that zinc homeostasis in the prostate is essential to prostate health, though the exact mechanisms are unclear. One theory proposes that dysregulation of zinc transporters in the prostate leads to disruption of zinc homeostasis and contributes to the formation of malignancies. Low intracellular zinc is often found in human prostate cancer tissues or in prostate epithelial cancer cell lines.[21,22]



Zinc is essential for:

- general metabolism
- growth and reproduction
- reproductive health
- cellular structure and function
- over 2000 transcription factors
- cellular metabolism
- cell-signaling
- cell cycle health
- cell mitosis and apoptosis
- DNA structural integrity
- DNA synthesis
- DNA replication and repair
- immune response
- prostate health
- synthesis and secretion of hormones

Healthy zinc levels are found to inhibit NF-kB (nuclear factor kB) activation in human prostate cancer cells. This sensitizes the cells to TNF (tumor necrosis factor) mediated apoptosis, and downregulates expression of VEGF, IL-8, and metalloproteinase-9 factors.[23]

CELLULAR HEALTH

Zinc, vital for many aspects of cellular health and cellular function, exerts cyto-protective influence through multiple pathways. Zinc influences all phases of the cell cycle and plays a key role in apoptosis.[3,4,7,22] Zinc helps maintain intracellular ion homeostasis.[3] It also exerts powerful anti-inflammatory and antioxidative influence.[3,4,7,13,22] Zinc is integral to proteins and transcription factors that regulate cellular functions including response to oxidative stress, DNA replication, DNA repair, and cell cycle health. Zinc is found to be a messenger in signal transduction and to play a critical role in gene expression.

Zinc acts as a signaling molecule both extracellularly (as in neurotransmitters) and intracellularly (as in calcium second-messenger systems). Thus, zinc deficiency is found to disrupt cell signaling.[3,7]

Since it is essential to the enzyme systems that influence cell division and proliferation, zinc is a key player in regulating cell proliferation. Decrease or absence of zinc from the extracellular milieu results in decreased activity of enzymes that regulate the cell cycle. It is thought that zinc may regulate DNA synthesis through these enzyme systems.[24]

Zinc coordinates mitosis and apoptosis. Zinc plays a major role in apoptosis, a process vital to cellular homeostasis. Zinc is found to be a major mechanism that contributes to cell death in response to toxins and disease. It is thought that altered cell susceptibility to apoptosis contributes to pathophysiological changes.[25]

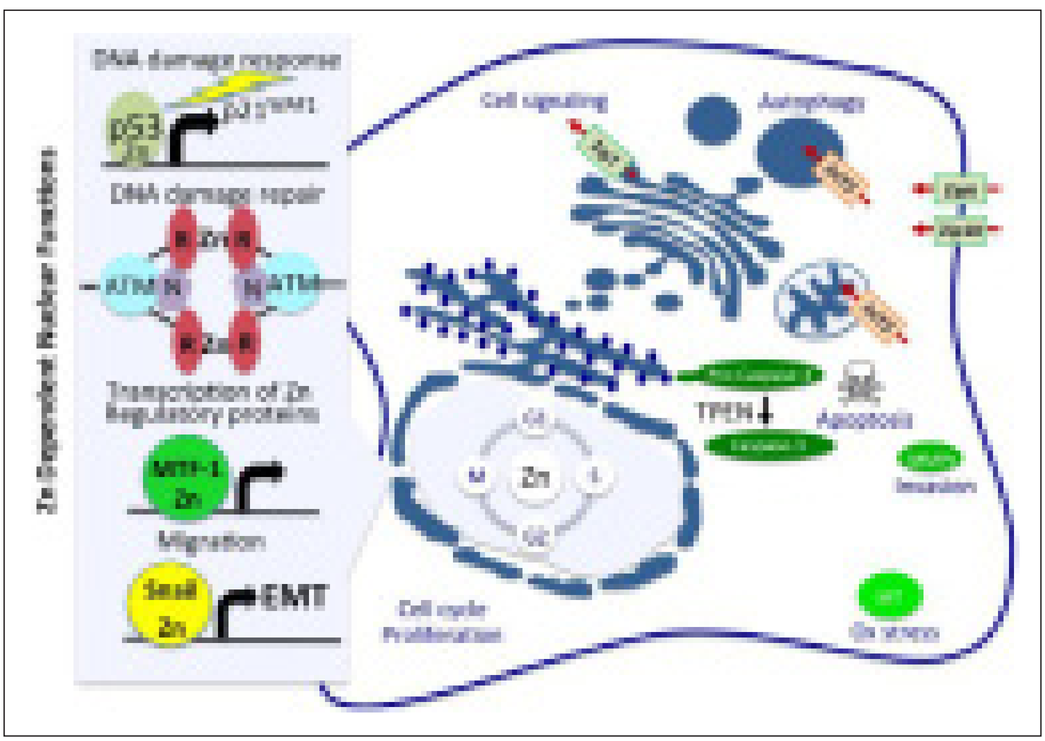
The pituitary is found to contain higher concentrations of zinc than other organs and zinc is found to enhance pituitary function.[24] Zinc is also found to influence hormonal regulation of cell division. It does this through its influence on the pituitary growth hormone known as IGF-1, which is sensitive to zinc.

When zinc is deficient, GH (growth hormone) can either increase or decrease, but circulating IGF-1 levels are seen to decrease consistently. Zinc is found to influence hormone signaling, membrane signaling systems, and intracellular second messengers that coordinate cell proliferation in response to IGF-1. IGF-1 mediates many cellular activities, including activation of amino acid and glucose uptake and regulation of the cell cycle.[24]

Zinc is also found in nerve cells and in membrane-enclosed synaptic vesicles.[2,3,22] It contributes to multiple biological processes including gene expression, DNA synthesis, enzymatic catalysis, hormonal storage and release, neurotransmission, memory, and the visual process.[25]

Zinc is essential for the metabolism of melatonin which plays a key role in dopamine regulation. Zinc deficiency is found in many children diagnosed with ADHD and is being investigated for its possible benefits through its ability to support dopamine pathways. Zinc is also a coenzyme for the enzymes that support anabolism of the polyunsaturated long-chain fatty acids (linoleic and linolenic acids), which are part of the neuronal membrane.[17,18]

Zinc exerts cyto-protective influence in the liver through its capacity to inhibit free radical formation and prevent lipid peroxidation. It influences metabolism of nutrients and steroids in the liver. The livers of zinc deficient rats showed a higher aromatization of testosterone to estradiol than the control groups with significantly lower serum levels of testosterone, estradiol, and LH (leutenizing hormone).[4]



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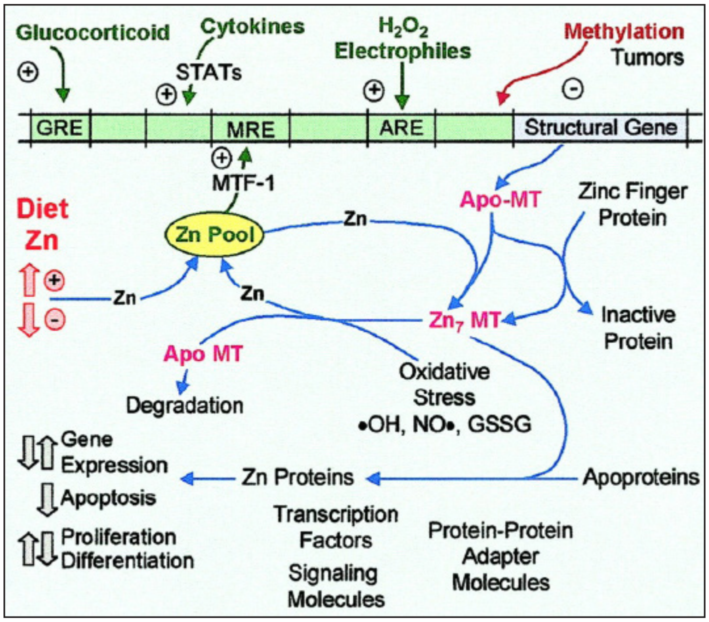


Overview of metallothionein (MT) gene regulation and function.
Davis SR, Cousins RJ. *Metallothionein expression in animals: a physiological perspective on function.* J Nutr. 2000. 130:1085-1088.

IMMUNE SYSTEM

Zinc is well-known for its significant role in immune response and immune health. It enhances both innate and adaptive immunity and is vital for immune cell function. Zinc is crucial for the formation and modulation of inflammatory processes. Deficiency leads to impaired immune function and promotes systemic inflammation. Zinc is found to be essential for immune cell development and to maintain activity of immune cells including neutrophils, monocytes, macrophages, NK cells, B cells, and T cells.[1,4,8,26]

Zinc is found to act as an anti-inflammatory and antioxidant.[11,12,27-29] In vitro and in vivo studies show that zinc deficiency leads to decreased oxidative stress and DNA damage.[22] In studies with both young adults and elderly subjects, oxidative stress markers and generation of inflammatory cytokines decreased with supplementation of zinc.[11,29]

ELDERLY / HEALTHY AGING

The natural aging process is associated with multiple changes that influence molecular and epigentic mechanisms. Changes commonly seen in the elderly include increased oxidative stress, decreased immune response, and systemic low-grade chronic inflammation. A significant amount of the elderly population is found to be zinc deficient due to inadequate intake along with a natural decline in zinc with aging. Studies find that zinc supplementation can help support immune response and healthy aging in the elderly population.[26,30]

Zinc deficient patients are found to have an increased incidence of congestive cardiopathy, respiratory infections, gastrointestinal disease, and depression. The decline of zinc status with age is most often correlated with decreased immune function in the elderly. Several studies reported reduced incidence of infections over the course of a year with zinc supplementation.[8]

Zinc is recognized as an effective anti-inflammatory and antioxidant. In studies with elderly subjects, zinc supplementation was found to decrease incidence of infections, increase plasma zinc, and decrease TNF (tumor necrosis factor) and oxidative stress markers in subjects given zinc compared to placebo group.[30]

Zinc is found to benefit T-cell function and to increase T-cell numbers in studies done with elderly subjects. Zinc intake yielded positive benefits in cognitive performance in 260 subjects aged 65 to 90 years and in other studies enhanced cognitive performance, stress response, and mood.[8] Studies show that zinc supplementation helps reduce progression of age-related macular degeneration.[3,31-34]

Nutritional status, including that of zinc, is found to impact development of and recovery from disease. Since zinc plays pivotal roles in cellular health, signal transduction, gene expression, mineral homeostasis and more, it is highly-researched for its role in cancer formation and cancer prevention. Low zinc levels in blood and tissues and dysregulation of zinc transporters and zinc transport proteins are implicated in many types of cancer including prostate, head and neck, breast, gall bladder, lung, and colon, among others.[3,7,35-43]

ZINC HOMEOSTASIS – POOLS AND TRANSPORTERS

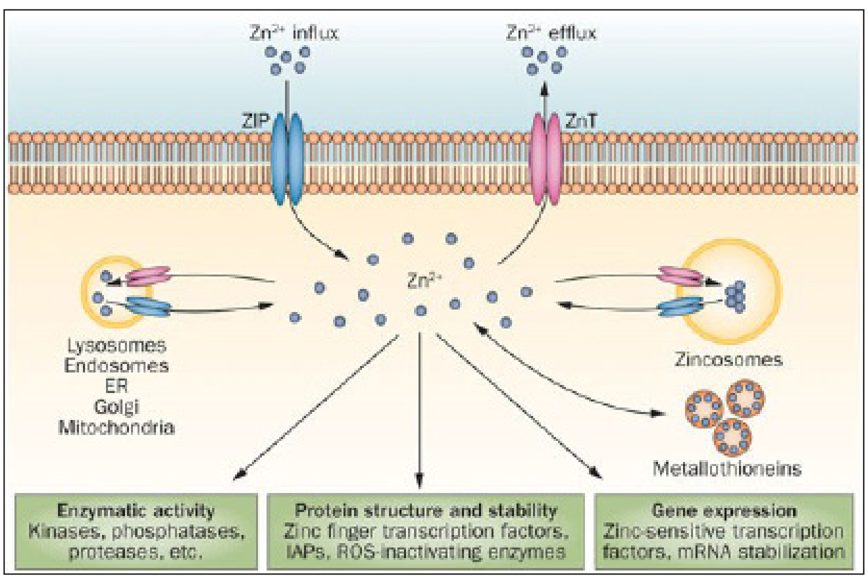
The body maintains zinc homeostasis by conserving intracellular zinc reserves along with other strategies. It is thought these pools of zinc reserves are stored in the Golgi or in other organelles of the cell. Often zinc reserves include zinc bound to metallothionein.[13] Mechanisms to maintain zinc homeostasis include maintenance of zinc pools and zinc transport systems. Subcellular zinc pools are maintained for the functional and structural integrity of cells.[24]

Zinc metabolism and homeostasis involve sophisticated mechanisms. When zinc is taken up by the cells it is distributed to the cytoplasm (50%), nucleus (30% to 40%), and cell membrane (10%). Once in the cell, zinc can either play a role in intracellular zinc storage or bind with proteins or enzymes. Zinc binds with metalloproteins to form structural components or with metalloenzymes which act as cofactors in many pathways.[44] Proteins known as metallothioneins (MT), Zrt- and Irt-like proteins (ZIP), and Zn transporters (ZnT) are key components in zinc metabolism and homeostasis.[44-46]

Zinc transporters help regulate intracellular zinc levels and play a key role in zinc homeostasis.[45] Members of the ZIP gene family transport numerous cations including zinc and other minerals. They are controlled by nutrient availability.[44] The ZIP and ZnT transporters are involved with moving zinc across cellular membranes (in and out of cells), and in moving zinc in and out of zinc pools, (reservoirs), where zinc is stored for later use.[47, 48]

The ZIP family (with about 14 members) facilitates the influx of zinc into the cytosol from the extracellular and intracellular compartments. The ZnT family (about 9 members) facilitates zinc's return from the cytosol into the extracellular and intracellular compartments.[47,49]

Zinc transporter dysfunction is found to be related to disrupted zinc homeostasis and consequent onset and progression of immune system impairment, chronic and neuro-generative diseases, and multiple other diseases.[47,48] Research suggests that measures of metallothionein or of cellular zinc transporters may give a more accurate picture of the zinc status of an individual.[13]



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Food-Grown from *S. cerevisiae*

Zinc grown in a food matrix offers excellent bioavailability and delivery into the cells for utilization. Food-grown zinc is also rich in proteins, peptides, and amino acids.[55] Studies confirm that mineral-enriched yeast is more biologically available than other forms. Studies with rats found zinc-enriched yeast (ZnY) to be 3.7 more times bioavailable than zinc gluconate.[50] Other studies show ZnY to be significantly more bioavailable than zinc chelate and zinc orotate.[51,52] In human studies, the net zinc balance in healthy humans, as measured through collection of urine, blood, and fecal samples, was significantly higher in those taking ZnY than in those taking zinc gluconate salts.[53,54]

Another study compared and evaluated the pharmacokinetics and biodistribution of ZnY and zinc sulfate in rats. In this study, bone was found to have the highest zinc level of all tissues and ZnY was found to have significantly higher bioavailablilty.[55]

Food-Grown Nutrients Deliver Bioavailable, Effective Nutrition

Whole foods contain a complex array of vitamins, minerals, phytochemicals, enzymes, and other beneficial compounds. These essential nutrients and cofactors enhance cellular health, cell-signaling, enzyme system response, and other activities that support physiological homeostasis.

- Improved Absorption
- Targeted Delivery
- Enhanced Utilization

Food-grown nutrients are delivered in the context of a whole food matrix that facilitates their bioavailabilty. This matrix includes peptide carriers and cofactors naturally occurring in foods that act as chaperones, delivering nutrients to the cells and tissues of the body. Human physiology is designed to obtain nutrients from plants and natural foods. Food-grown nutrients are designed to emulate whole foods while delivering a higher concentration of specific vitamins or minerals.

Yeast Medium

There are numerous studies on the uptake of trace metals by the yeast *Saccharomyces cerevisiae* because of its ability to take up and incorporate nutrients into its structure. This yeast is of great interest to scientists for many reasons. One reason is due to its high nutritional content that benefits both humans and animals.[56] Food-grown Zinc, grown on *Saccharomyces cerevisiae*, contains various immune-enhancing compounds such as β-glucan, nucleic acids, mannan oligosaccharides, and chitin.[57]

Study of *S. cerevisiae* yeast has been instrumental in helping scientists discover and understand mineral transport systems. This yeast is found to be an ideal delivery vehicle for mineral supplements because of its ability to incorporate metals into its cells. This is attributed to the high concentration of proteins in yeast. *S. cerevisiae* yeast is able to accumulate metal ions from aqueous solutions through several mechanisms and can incorporate substantial amounts of minerals into its structure.[57,58]

For more information on any of the ingredients listed here, including extensive research or individual monographs compiled by Donnie Yance, please email info@naturaedu.com.

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