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A review on role of zinc deficiency in humans and its rectification through Horti-agro food supplements

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Abstract
Zinc being an essential micro element whose increasing significance to health is highly appreciated. Zinc is found in over 200 enzymes and hormones in mankind. Zinc is a natural element found in all plants and animals and plays a crucial part and integral as well as vital component in the health of our skin, teeth, bones, hair, nails, muscles, nerves and brain function. Zinc is responsible for numerous and multifaceted functions in human metabolism. Severe zinc deficiency leads to increased susceptibility to variety of pathogens. The human health problems aggravated by zinc deficiency leads to complications of pregnancy and childbirth, low birth weight and poor growth in childhood, reduced immune competence and increased infectious disease morbidity. The complications arising in pregnant women suffering with zinc deficiency are at higher risk of premature and inefficient labor and miscarriages, labor and delivery, stillbirths, lower mental ability of the child, retarded fetal growth and poor immunity of both mother and neo-infant. Trace element zinc imparts a sturdy role in maintaining the healthy growth of the human body, especially for infants and young children's growth and development. It is pragmatically used to control the enzymes that operate and renew the cells in our bodies. Zinc deficiency is an important public health problem gaining recognition recently, nutritionists have been concerned that zinc deficiency affects large numbers of women and children in India and worldwide. Well planned vegetarian diets can provide adequate amounts of zinc from varied plant sources. The incorporating ingredients readily available for good sources of zinc for vegetarians include legumes, nuts, seeds, fortified breakfast, fruits and vegetables. Sulphur plays an important role in rendering zinc absorptions binding sites. Sulphur-containing amino acids e.g. cysteine and methionine, found in a range of seeds, nuts, and vegetables and hydroxy acids e.g. citric acid found in citrus fruits, malic acid in apples and tartaric acid in grapes, bind to zinc conveniently and enhance its absorption. Various available organic acids that are present in foods or produced during fermentation can also enhance zinc absorption. This review concerns the vital importance and pivotal role of zinc in health and the possible implications and consequences of its deficiency and possible remedial measures through utilization of various available horticultural products and food supplements imparting zinc to human metabolism.

Keywords: Zinc**,** phytates, deficiency, gluconates**,** labor

Introduction
The importance of micronutrients in health and nutrition is indisputably recognized across the globe and among them, zinc is an essential element whose critical significance to human health wellness is increasingly appreciated and whose deficiency may play an important role in the manifestation of diseases. Zinc is an essential mineral that is naturally present in some horticultural foods, fortified to other food sources and being available as a dietary supplement in the form of medicines. Zinc is also found in many cold lozenges prevalent in market and some over the drugs counter being sold as cold remedies. Zinc is a trace mineral essentially supportive to all forms of life because of its fundamental role in gene expression, cell development and replication. Nearly two billion people in the developing world encompassing African and Asian countries are deficient in zinc and suffering as reported by Prasad (2003) [19]. Severe or clinical zinc deficiency was defined last century, as a condition characterized by short stature, hypogonadism, impaired immune function, skin disorders, cognitive dysfunction and anorexia. Nutritionists have long been concerned that zinc deficiency affects large numbers of women and children worldwide. Several studies have now confirmed that zinc deficiency in the developing countries is fairly prevalent and gets unnoticed whereas growth retardation commonly observed in these countries may be ascribed to zinc deficiency as envisaged by Brown *et al.*, (2002) [3]. Zinc deficiency was indicated as a risk factor for immune deficiency and susceptibility to infection in the elderly which leads to ageing aliments. Inadequate stores of zinc might be a risk factor of pneumonia in the elderly people as reported

by Meydani *et al.,* (2007) [17]. Due to the wide prevalence of zinc deficiency and the multitude of zinc's essential biological functions, nutritional rectification of zinc deficiency may have a significant impact on different aspects of human health. For this reason, it is important to attempt to quantify the prevalence of zinc deficiency and its broad contribution to the global burden of disease. An insight of this chapter is to describe the quantum, distribution and disease burden implications of zinc deficiency.

Major Causes of Zinc Deficiency

People with gastrointestinal and other diseases

About 70 per cent of zinc in circulation is bound to the blood protein albumin. Any situation that affects the albumin concentrations has a consequential secondary effect on the body's zinc levels. Naber *et al.,* (1998) [18] reported that the people who have undergone gastrointestinal surgery and digestive disorders can decrease zinc absorption and increase endogenous zinc losses primarily from the gastrointestinal tract and to a lesser extent from the kidney. Other diseases associated with zinc deficiency include malabsorption syndrome, chronic liver disease, chronic renal disease, sickle cell disease, diabetes, malignancy, and other chronic illnesses. Prasad (2004) [20] reported that increased motility decreases the success of digestion and absorption and severe diarrhea also leads to excessive loss of zinc.

Vegetarians

Hunt *et al.,* (2003) [11] reported that the bioavailability of zinc from vegetarian diets is lower and to a lesser extent than from non-vegetarian diets because vegetarians do not eat meat, which is high in bioavailable zinc and may enhance zinc absorption. In addition, vegetarians typically eat high levels of legumes and whole grains, which contain phytates that bind zinc and inhibit its absorption. Vegetarians sometimes require as much as 50% more of the RDA for zinc than non-vegetarians. In addition, they might benefit from using certain food preparation techniques that reduce the binding of zinc by phytates and increase its bioavailability. Techniques to increase zinc bioavailability include soaking beans, grains, and seeds in water for several hours before cooking them and allowing them to sit after soaking until sprouts form. Vegetarians can also augment their zinc intake by consuming more leavened grain products (such as bread) than unleavened products because leavening partially breaks down the phytate; thus, the body absorbs more zinc from leavened grains than unleavened grains.

Low albumin persists in conditions in which the body does not properly absorb and digest protein or in disease where considerable chunks of proteins are lost through diarrhea. Synthesis of albumin occurs in liver, so any liver disease can also negatively affect zinc levels.

Pregnant and lactating women

Caulfield *et al.,* 1998 [4] reported that pregnant women, particularly those starting their pregnancy with marginal zinc status, are at higher risk of becoming zinc insufficient due, in part, to high fetal requirements for zinc. Lactation can also deplete maternal zinc stores. For these reasons, the RDA for zinc is higher for pregnant and lactating women than for other women. Sub-optimal levels of zinc on pregnant woman have serious implications on health issues both of infant and mother.

Older infants who are exclusively breastfed

Breast milk provides sufficient zinc (2 mg/day) for the first 4–6 months of life but does not provide recommended amounts of zinc for infants aged 7–12 months, who need 3 mg/day. In addition to breast milk, infants aged 7–12 months should consume age-appropriate foods or formula containing zinc. Zinc supplementation has improved the growth rate in some children who demonstrate mild-to-moderate growth failure and who have a zinc deficiency. The problem is more severe in less protected environments with high infections burden and limited dietary options and intake.

People with sickle cell disease

Results from a large cross-sectional survey suggest that 44% of children with sickle cell disease have a low plasma zinc concentration as investigated by Leonard *et al.,* (1998) [15], possibly due to increased nutrient requirements and/or poor nutritional status as reported by Zemel *et al.,* (2002) [26]. Zinc deficiency also affects approximately 60%–70% of adults with sickle cell disease. Zinc supplementation has been shown to improve growth in children with sickle cell disease.

Alcoholics

Approximately 30%–50% of alcoholics have low zinc status because ethanol consumption decreases intestinal absorption of zinc and increases urinary zinc excretion. In addition, the variety and amount of food consumed by many alcoholics is limited, leading to inadequate zinc intake as reported by Menzano *et al.,* (1994) [16].

Table 1: Recommended Dietary Allowances (RDAs) for Zinc

Age	Male	Female	Pregnancy	Lactation
0–6 months	2 mg*	2 mg*	-	-
7–12 months	3 mg	3 mg	-	-
1–3 years	3 mg	3 mg	-	-
4–8 years	5 mg	5 mg	-	-
9–13 years	8 mg	8 mg	-	-
14–18 years	11 mg	9 mg	12 mg	13 mg
19+ years	11 mg	8 mg	11 mg	12 mg

***Source*:** Institute of Medicine, Food and Nutrition Board (2001) [27].

Sources of Zinc

Major plant sources of zinc include cooked dried beans, sea vegetables, fortified cereals, soyfoods, nuts, peas, seeds, mushrooms, day lily flowers, edible fungus, cabbage, black sesame, black rice, dates, hazelnuts, ebony and other vegetables, food crops and fruits. Traditional staple foods, such as cereals, legumes and tubers contain zinc but the presence of phytate, fiber, and lignin reduces its bioavailability. These substances form insoluble complexes with zinc, preventing its absorption. The recommended dietary allowances (RDAs) for zinc for male, female according to age groups are presented in table 1 as recommended by Institute of Medicine, Food and Nutrition Board (2001) [27]. Vegetables and fruits contribute very little to dietary zinc intake, but fruits eaten with cereals may increase the bioavailability of zinc as reported by Walsh *et al.,* (2007) [23]. The concentration of zinc in plants varies based on levels of the element in soil. When there is adequate zinc in the soil, the food plants that contain the most zinc are wheat and various seeds e.g. sesame, poppy, alfalfa, celery and mustard. Zinc is also found in beans, nuts, almonds, whole grains, pumpkin seeds, sunflower seeds and blackcurrant.

Millions of people throughout the world may have inadequate levels of zinc in the diet due to limited access to zinc-rich foods and the abundance of zinc inhibitors, such as phytates and other inhibitors common in plant-based diets as reported by Sandstead *et al.*, (1991) [21]. Wikoff and Castle (1993) [25] reported that calcium can retard zinc absorption, so calcium and zinc supplements should be taken separately at different times of the day. Coffee is known to contain tannin which can potentially inhibit zinc absorption. Because zinc is not well conserved in the body and because zinc deficiency is directly related to dietary zinc intake, an indirect approach to quantify the prevalence of zinc deficiency would be to examine the adequacy of zinc in the diet in various regions. Dietary supplements contain several forms of zinc, including zinc gluconate, zinc sulphate and zinc acetate. The percentage of elemental zinc varies by different forms available from plant sources are presented in table 2.

Table 2: Food derived from Plants Zinc per 100 g

Sun-dried tomatoes	136 mg
Zinc-fortified breakfast cereals	1.9–7.8 mg
Pumpkin seeds	7.5 mg
Sunflower seeds	5.8 mg
Sesame seeds	5.5 mg
Pine nuts/cashews	5.3-5.5 mg
Sausage, vegetarian, zinc fortified	4.4 mg
Flaxseed	4.3 mg
Almonds/pecans/brazil nuts	3.7-4.1 mg
Lentils/soy beans/kidney beans, dried	3.0-4.0 mg
Whole wheat biscuit breakfast cereal	2.0-2.7 mg
Bread roll, mixed grain, toasted	2.0 mg

Source: From Food Standards Australia New Zealand. NUTTAB 2010 [6] online searchable database.

Table 3: Food, serving size zinc per serve

Brown rice, cooked, 1 cup	1.9 mg
Tofu, firm, 100 g	1.7 mg
Cashews, 30 g	1.7 mg
Lentils 3/4 cup	1.6 mg
Pine nuts 30 g	1.6 mg
Sundried tomatoes 1 tablespoon (11.2 g)	1.5 mg
Green peas, frozen, (1/2 cup)	1.5 mg
Soybeans cooked/canned (1/2 cup)	1.3 mg
Zinc-fortified breakfast cereals, 1/2 cup	1.2 mg
Pumpkin seeds 1 tablespoon (15 g)	1.2 mg
Pecans 30 g	1.2 mg
Brazil nuts 30 g	1.2 mg
Egg whole	1.2 mg
Almonds 30 g	1.1 mg
Cow's milk 1 cup (250 ml)	0.9 mg
Sunflower seeds 1 tablespoon (15 g)	0.9 mg
Mixed-grain bread	2 slices 0.7mg
Whole meal bread	2 slices 0.6mg
Cocoa powder 1 tablespoon (7 g)	0.6 mg
Peanut butter 3 teaspoons (15 g)	0.5 mg

Source: From Food Standards Australia New Zealand. AUSNUT 2007 online searchable database.

Role of zinc in health and disease

Zinc being an essential trace mineral, is required for the metabolic activity of 300 of the body's enzymes, and is considered essential for cell division and the synthesis of DNA and protein. These enzymes are involved with the metabolism of protein, carbohydrate and fat. Zinc is also critical to tissue growth, wound healing, taste acuity, connective tissue growth and maintenance, immune system function, prostaglandin production, bone mineralization, proper thyroid function, blood clotting, cognitive functions, fetal growth and sperm production. Zinc is necessary to maintain normal serum testosterone. Inadequate zinc levels prevent the pituitary gland from releasing luteinizing and follicle stimulating hormones, which stimulate testosterone production. Zinc also inhibits the aromatase enzyme that converts testosterone into excess estrogen. Higher estrogen activity results in increased risk of heart disease, weight gain, and obesity. One reason for the progressive weight gain with age is that fat cells contain aromatase. More fat cells mean more estrogen which means more fat deposition. This is further aggravated by alcohol consumption, which lowers zinc and increases estrogen, and so magnifies the problem. In addition to the impact on hormone levels, zinc also has been proven to help the body produce healthier sperm by increasing sperm count and motility. Zinc deficiency was indicated as a risk factor for immune deficiency and susceptibility to infection in the elderly. Zinc is essential for the immune system and zinc deficiency has dramatic implications for immune function. Zinc is a component in thymic hormone which controls and facilitates the maturation of lymphocytes. Fortes *et al.*, (1998) [8] emphasizes that zinc also plays a role in cell division and DNA replication, thereby aiding in the production of immune system cells. Zinc supplementation has been shown to improve the cell-mediated immune response of healthy elderly. Zinc is essential for healthy skin. Topical zinc preparations (zinc oxide) have been used as an astringent to treat diaper rash, itching and chapped lips and skin. Zinc sulfate in a water based solution has been used for treating acne, cold sores and burns. Internally, zinc stimulates cell division, healing, proper connective tissue formation, and increases the transport of Vitamin A from the liver to the skin, helping to protect body tissue from damage and repair any damage present. Zinc is found in the vesicles of the mossy fiber system of the brain's hippocampus. These fibers play a role in enhancing memory and thinking skills. Zinc activates areas of the brain that receive and process information from taste and smell sensors. Levels of zinc in plasma were found to influence appetite and taste preference. Insufficient zinc has been linked to anorexia, which responds well to zinc replacement treatment. The deficiency symptoms of zinc include growth retardation, low blood pressure, retarded bones, loss of appetite, loss of sense of smell and taste, weight loss, pale skin, diarrhea, hair loss, Fatigue, white spots under finger nails. Inadequate stores of zinc might be a risk factor of pneumonia in the elderly. Zinc deficiency contributes to increased risk of incidence for important childhood diseases that are predominant causes of death among children. Zinc deficiency increases the risk of severity and death during illness with diarrhea or pneumonia. Shankar *et al.*, (1998) [22] highlighted that maternal or gestational zinc deficiency may affect immunological development in the newborn in ways that compromise immune function throughout the lifespan irrespective of zinc status. Hulisz (2004) [10] reported that zinc is effective in shortening the duration of the common cold, if it is administered no later than 24 h within the onset of the symptoms. It is well known that zinc deficiency is widespread in developing countries encompassing African continent with particular effects in pregnancy and early childhood. Evidence is accumulating that this deficiency leads to complications of pregnancy and childbirth, lower birth weight and poor growth in childhood, reduced immune-competence, and increased infectious

disease morbidity. Pregnant women with zinc deficiency are at higher risk of premature labor and miscarriages, inefficient labor and delivery, stillbirths, lower mental ability of the child, retarded fetal growth and low immunity of both mother and baby. Since childhood infectious disease morbidity from diarrhea, pneumonia, and malaria is the cause of most of the childhood deaths in developing countries, it is also plausible that zinc deficiency contributes to the elevated mortality rates still seen in many developing countries. Zinc deficiency leads to increased risk of maternal and neonate morbidity and mortality. Maternal nutrition status is an important determinant of perinatal and neonatal well-being. Krebs (1998) [14] reported that the lactation period poses a different threat to maternal zinc homeostasis because zinc requirements during this period are very high. Chronic diarrhea causes zinc deficiency, and zinc deficiency in turn can contribute to diarrhea. Christa *et al.,* (2006) [5] investigated that zinc treatment has been shown to decrease the severity of the diarrhoea episode by decreasing the number of stools per day, the volume of stools per day, and the number of episodes lasting beyond 7 days. Zinc supplementation in the treatment of childhood diarrhea was well tolerated by patients. Zinc helps in maintaining the integrity of skin and mucosal membranes as revealed by Wintergerst *et al.,* (2007) [24]. Patients with chronic leg ulcers have abnormal zinc metabolism and low serum zinc levels, and clinicians frequently treat skin ulcers with zinc supplements. All body tissues contain zinc; In skin, it is five to six times more concentrated in the epidermis than the dermis. Zinc is also an anti-inflammatory agent. These unique properties of zinc may have significant therapeutic benefits in several diseases in humans. Zinc is a critical nutrient for central nervous system development which occurs during pre- and postnatal life. Because of the important role of zinc in central nervous system function, it is clear that maternal and early infant zinc deficiencies are likely to adversely affect fetal and infant neurologic and behavioral development. There is evidence associating zinc deficiency with deficits in activity, attention, and motor development and thus interfering with cognitive performance in humans; however, there is no clear explanation of the mechanisms underlying this relation. In humans, severe zinc deficiency can cause abnormal cerebellar function and impair behavioral and emotional responses as reported by Balck (1998) [1]. The effects of zinc on maternal health and pregnancy outcomes have been studied in multiple observational and interventional studies. Branda *et al.,* (1995) [2] reported the importance of zinc in bone metabolism. Zinc is intimately linked to bone metabolism, thus, zinc acts positively on growth and development. Zinc concentration in bone is very high compared with that in other tissues, and it is considered an essential component of the calcified matrix. Zinc also enhances vitamin D effects on bone metabolism through the stimulation of DNA synthesis in bone cells. Zinc gluconate lozenges taken at the first sign of a cold reduce duration and symptom severity. Zinc, perceived as an antiviral agent and astringent, is released into the saliva, relieving cough, nasal drainage and congestion. Zinc abnormalities also often exist in mood disorder patients. Zinc sulfate when taken as a supplement appears effective in reducing fatigue, mood swings and changes in appetite.

Health risks from excessive zinc

Zinc toxicity due to acute or chronic ingestion of high quantities of zinc supplements can also occur and lead to impaired immune response, hypocupremia, microcytosis, and neutropenia. Zinc toxicity can occur in both acute and chronic forms. Acute adverse effects of high zinc intake include nausea, vomiting, loss of appetite, abdominal cramps, diarrhea, and headaches. The doses of zinc 80 mg per day in the form of zinc oxide for 6.3 years, on average have been associated with a significant increase in hospitalizations for genitourinary causes, raising the possibility that chronically high intakes of zinc adversely affect some aspects of urinary physiology as reported by Johnson *et al.,* (1998). Intakes of 150–450 mg of zinc per day have been associated with such chronic effects as low copper status, altered iron function, reduced immune function, and reduced levels of high-density lipoproteins as investigated by Hooper *et al.,* (1980) [9]. Reductions in a copper-containing enzyme, a marker of copper status, have been reported with even moderately high zinc intakes of approximately 60 mg/day for up to 10 weeks.

Conclusion and future directions

Zinc is an essential mineral element which human cannot synthesis by its own. Zinc is an essential micronutrient for human health next after iron and plays an essential role as a defensive mechanism in combating diarrhea, pneumonia, common cold, respiratory infections and malaria. Sufficient zinc is essential in maintaining immune system function. The role of zinc in cell division, cell wall growth, wound healing and breakdown of carbohydrates cannot be undermined. Supplementation of zinc and with other micronutrients may be beneficial during periods of greatest vulnerability such as early childhood, pregnancy and elderly. Young people also have very high zinc requirements to maintain skeletal maturation, especially in females after menarche and during pregnancy. Zinc has many actions that may promote debridement and wound healing in patients suffering from burns. Ensuring adequate levels of zinc intake should be a key component in efforts to reduce illness. Zinc intake is a challenge for vegetarian peoples. With good planning, vegetarians can consume enough zinc from various horticultural products such as nuts, seeds as well as through proper intake of fruits and vegetables. Overall, zinc intakes from vegetarian diets are either similar to or lower than non-vegetarian diets. Because phytate or other dietary inhibitors in vegetarian diets typically decrease zinc absorption, there is normally a compensatory improved efficiency of absorption and excretion of zinc. It is essential to educate, inform and motivate lower intake of zinc human communities to modify the diet for inclusion of animal products and various horticultural sources that enhance zinc absorption which are rich in zinc. Zinc deficiency can be countered by dietary modifications, diversification, supplementation and bio-fortification depending upon the resources availability. Lower intake of zinc in humans a t different growth stage may result in growth failure.

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