NIH Office of Dietary Supplements

Zinc

Fact Sheet for Health Professionals

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Introduction

Zinc is an essential mineral that is naturally present in some foods, added to others, and available as a dietary supplement. Zinc is also found in many cold lozenges and some over-the-counter drugs sold as cold remedies.

Zinc is involved in numerous aspects of cellular metabolism. It is required for the catalytic activity of approximately 100 enzymes [1,2] and it plays a role in immune function [3,4], protein synthesis [4], wound healing [5], DNA synthesis [2,4], and cell division [4]. Zinc also supports normal growth and development during pregnancy, childhood, and adolescence [6-8] and is required for proper sense of taste and smell [9]. A daily intake of zinc is required to maintain a steady state because the body has no specialized zinc storage system [10].

Recommended Intakes

Intake recommendations for zinc and other nutrients are provided in the Dietary Reference Intakes (DRIs) developed by the Food and Nutrition Board (FNB) at the Institute of Medicine of the National Academies (formerly National Academy of Sciences) [2]. DRI is the general term for a set of reference values used for planning and assessing nutrient intakes of healthy people. These values, which vary by age and gender [2], include the following:

- Recommended Dietary Allowance (RDA): average daily level of intake sufficient to meet the nutrient requirements of nearly all (97%–98%) healthy individuals.
- Adequate Intake (AI): established when evidence is insufficient to develop an RDA and is set at a level assumed to ensure nutritional adequacy.
- Tolerable Upper Intake Level (UL): maximum daily intake unlikely to cause adverse health effects [2].

The current RDAs for zinc are listed in Table 1 [2]. For infants aged 0 to 6 months, the FNB established an AI for zinc that is equivalent to the mean intake of zinc in healthy, breastfed infants.

Table 1: Recommended Dietary Allowances (RDAs) for Zinc [2]

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

* Adequate Intake (AI)

Sources of Zinc

Food

A wide variety of foods contain zinc (Table 2) [2]. Oysters contain more zinc per serving than any other food, but red meat and poultry provide the majority of zinc in the American diet. Other good food sources include beans, nuts, certain types of seafood (such as crab

and lobster), whole grains, fortified breakfast cereals, and dairy products [2,11].

Phytates—which are present in whole-grain breads, cereals, legumes, and other foods—bind zinc and inhibit its absorption [2,12,13]. Thus, the bioavailability of zinc from grains and plant foods is lower than that from animal foods, although many grain- and plant-based foods are still good sources of zinc [2].

Table 2: Selected Food Sources of Zinc [11]

Food	Milligrams (mg) per serving	Percent DV*
Oysters, cooked, breaded and fried, 3 ounces	74.0	493
Beef chuck roast, braised, 3 ounces	7.0	47
Crab, Alaska king, cooked, 3 ounces	6.5	43
Beef patty, broiled, 3 ounces	5.3	35
Breakfast cereal, fortified with 25% of the DV for zinc, ¾ cup serving	3.8	25
Lobster, cooked, 3 ounces	3.4	23
Pork chop, loin, cooked, 3 ounces	2.9	19
Baked beans, canned, plain or vegetarian, ½ cup	2.9	19
Chicken, dark meat, cooked, 3 ounces	2.4	16
Yogurt, fruit, low fat, 8 ounces	1.7	11
Cashews, dry roasted, 1 ounce	1.6	11
Chickpeas, cooked, ½ cup	1.3	9
Cheese, Swiss, 1 ounce	1.2	8
Oatmeal, instant, plain, prepared with water, 1 packet	1.1	7
Milk, low-fat or non fat, 1 cup	1.0	7
Almonds, dry roasted, 1 ounce	0.9	6
Kidney beans, cooked, ½ cup	0.9	6
Chicken breast, roasted, skin removed, ½ breast	0.9	6
Cheese, cheddar or mozzarella, 1 ounce	0.9	6
Peas, green, frozen, cooked, ½ cup	0.5	3
Flounder or sole, cooked, 3 ounces	0.3	2

* DV = Daily Value. DVs were developed by the U.S. Food and Drug Administration to help consumers compare the nutrient contents of products within the context of a total diet. The DV for zinc is 15 mg for adults and children age 4 and older. Food labels, however, are not required to list zinc content unless a food has been fortified with this nutrient. Foods providing 20% or more of the DV are considered to be high sources of a nutrient.

The U.S. Department of Agriculture's (USDA's) Nutrient Database Web site [11] lists the nutrient content of many foods and provides a comprehensive list of foods containing zinc arranged by nutrient content and by food name.

Dietary supplements

Supplements contain several forms of zinc, including zinc gluconate, zinc sulfate, and zinc acetate. The percentage of elemental zinc varies by form. For example, approximately 23% of zinc sulfate consists of elemental zinc; thus, 220 mg of zinc sulfate contains 50 mg of elemental zinc. The elemental zinc content appears in the Supplement Facts panel on the supplement container. Research has not determined whether differences exist among forms of zinc in absorption, bioavailability, or tolerability.

In addition to standard tablets and capsules, some zinc-containing cold lozenges are labeled as dietary supplements.

Other sources

Zinc is present in several products, including some labeled as homeopathic medications, sold over the counter for the treatment and prevention of colds. Numerous case reports of anosmia (loss of the sense of smell), in some cases long-lasting or permanent, have been associated with the use of zinc-containing nasal gels or sprays [14,15]. In June 2009, the FDA warned consumers to stop using three zinc-containing intranasal products because they might cause anosmia [16]. The manufacturer recalled these products from the marketplace. Currently, these safety concerns have not been found to be associated with cold lozenges containing zinc.

Zinc is also present in some denture adhesive creams at levels ranging from 17–34 mg/g [17]. While use of these products as directed (0.5–1.5 g/day) is not of concern, chronic, excessive use can lead to zinc toxicity, resulting in copper deficiency and neurologic disease. Such toxicity has been reported in individuals who used 2 or more standard 2.4 oz tubes of denture cream per week [17,18]. Many denture creams have now been reformulated to eliminate zinc.

Zinc Intakes and Status

Most infants (especially those who are formula fed), children, and adults in the United States consume recommended amounts of zinc according to two national surveys, the 1988–1991 National Health and Nutrition Examination Survey (NHANES III) [19] and the 1994 Continuing Survey of Food Intakes of Individuals (CSFII) [20].

However, some evidence suggests that zinc intakes among older adults might be marginal. An analysis of NHANES III data found that 35%–45% of adults aged 60 years or older had zinc intakes below the estimated average requirement of 6.8 mg/day for elderly females and 9.4 mg/day for elderly males. When the investigators considered intakes from both food and dietary supplements, they found that 20%–25% of older adults still had inadequate zinc intakes [21].

Zinc intakes might also be low in older adults from the 2%–4% of U.S. households that are food insufficient (sometimes or often not having enough food) [22]. Data from NHANES III indicate that adults aged 60 years or older from food-insufficient families had lower intakes of zinc and several other nutrients and were more likely to have zinc intakes below 50% of the RDA on a given day than those from food-sufficient families [23].

Zinc Deficiency

Zinc deficiency is characterized by growth retardation, loss of appetite, and impaired immune function. In more severe cases, zinc deficiency causes hair loss, diarrhea, delayed sexual maturation, impotence, hypogonadism in males, and eye and skin lesions [2,8,24,25]. Weight loss, delayed healing of wounds, taste abnormalities, and mental lethargy can also occur [5,8,26-30]. Many of these symptoms are non-specific and often associated with other health conditions; therefore, a medical examination is necessary to ascertain whether a zinc deficiency is present.

Zinc nutritional status is difficult to measure adequately using laboratory tests [2,31,32] due to its distribution throughout the body as a component of various proteins and nucleic acids [33]. Plasma or serum zinc levels are the most commonly used indices for evaluating zinc deficiency, but these levels do not necessarily reflect cellular zinc status due to tight homeostatic control mechanisms [8]. Clinical effects of zinc deficiency can be present in the absence of abnormal laboratory indices [8]. Clinicians consider risk factors (such as inadequate caloric intake, alcoholism, and digestive diseases) and symptoms of zinc deficiency (such as impaired growth in infants and children) when determining the need for zinc supplementation [2].

Groups at Risk of Zinc Inadequacy

In North America, overt zinc deficiency is uncommon [2]. When zinc deficiency does occur, it is usually due to inadequate zinc intake or absorption, increased losses of zinc from the body, or increased requirements for zinc [26,27,34]. People at risk of zinc deficiency or inadequacy need to include good sources of zinc in their daily diets. Supplemental zinc might also be appropriate in certain situations.

People with gastrointestinal and other diseases

Gastrointestinal surgery and digestive disorders (such as ulcerative colitis, Crohn's disease, and short bowel syndrome) can decrease zinc absorption and increase endogenous zinc losses primarily from the gastrointestinal tract and, to a lesser extent, from the kidney [2,26,35,36]. Other diseases associated with zinc deficiency include malabsorption syndrome, chronic liver disease, chronic renal disease, sickle cell disease, diabetes, malignancy, and other chronic illnesses [37]. Chronic diarrhea also leads to excessive loss of zinc [24].

Vegetarians

The bioavailability of zinc from vegetarian diets is lower 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 [31,38].

Vegetarians sometimes require as much as 50% more of the RDA for zinc than non-vegetarians [2]. 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 [38]. Vegetarians can also increase their zinc intake by consuming more leavened grain products

(such as bread) than unleavened products (such as crackers) because leavening partially breaks down the phytate; thus, the body absorbs more zinc from leavened grains than unleavened grains.

Pregnant and lactating women

Pregnant women, particularly those starting their pregnancy with marginal zinc status, are at increased risk of becoming zinc insufficient due, in part, to high fetal requirements for zinc [39]. Lactation can also deplete maternal zinc stores [40]. For these reasons, the RDA for zinc is higher for pregnant and lactating women than for other women (see Table 1) [2].

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 [2,33]. In addition to breast milk, infants aged 7–12 months should consume age-appropriate foods or formula containing zinc [2]. Zinc supplementation has improved the growth rate in some children who demonstrate mild-to-moderate growth failure and who have a zinc deficiency [24,41].

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 [42], possibly due to increased nutrient requirements and/or poor nutritional status [43]. Zinc deficiency also affects approximately 60%–70% of adults with sickle cell disease [44]. Zinc supplementation has been shown to improve growth in children with sickle cell disease [43].

Alcoholics

Approximately 30%–50% of alcoholics have low zinc status because ethanol consumption decreases intestinal absorption of zinc and increases urinary zinc excretion [44]. In addition, the variety and amount of food consumed by many alcoholics is limited, leading to inadequate zinc intake [2,46,47].

Zinc and Health

Immune function

Severe zinc deficiency depresses immune function [48], and even mild to moderate degrees of zinc deficiency can impair macrophage and neutrophil functions, natural killer cell activity, and complement activity [49]. The body requires zinc to develop and activate T-lymphocytes [2,50]. Individuals with low zinc levels have shown reduced lymphocyte proliferation response to mitogens and other adverse alterations in immunity that can be corrected by zinc supplementation [49,51]. These alterations in immune function might explain why low zinc status has been associated with increased susceptibility to pneumonia and other infections in children in developing countries and the elderly [52-55].

Wound healing

Zinc helps maintain the integrity of skin and mucosal membranes [49]. Patients with chronic leg ulcers have abnormal zinc metabolism and low serum zinc levels [56], and clinicians frequently treat skin ulcers with zinc supplements [57]. The authors of a systematic review concluded that zinc sulfate might be effective for treating leg ulcers in some patients who have low serum zinc levels [58,59]. However, research has not shown that the general use of zinc sulfate in patients with chronic leg ulcers or arterial or venous ulcers is effective [58,59].

Diarrhea

Acute diarrhea is associated with high rates of mortality among children in developing countries [60]. Zinc deficiency causes alterations in immune response that probably contribute to increased susceptibility to infections, such as those that cause diarrhea, especially in children [49].

Studies show that poor, malnourished children in India, Africa, South America, and Southeast Asia experience shorter courses of infectious diarrhea after taking zinc supplements [61]. The children in these studies received 4–40 mg of zinc a day in the form of zinc acetate, zinc gluconate, or zinc sulfate [61].

In addition, results from a pooled analysis of randomized controlled trials of zinc supplementation in developing countries suggest that zinc helps reduce the duration and severity of diarrhea in zinc-deficient or otherwise malnourished children [62]. Similar findings were reported in a meta-analysis published in 2008 and a 2007 review of zinc supplementation for preventing and treating diarrhea [63,64]. The effects of zinc supplementation on diarrhea in children with adequate zinc status, such as most children in the United States, are not clear.

The World Health Organization and UNICEF now recommend short-term zinc supplementation (20 mg of zinc per day, or 10 mg for infants under 6 months, for 10–14 days) to treat acute childhood diarrhea [60].

The common cold

Researchers have hypothesized that zinc could reduce the severity and duration of cold symptoms by directly inhibiting rhinovirus binding and replication in the nasal mucosa and suppressing inflammation [65,66]. Although studies examining the effect of zinc treatment on cold symptoms have had somewhat conflicting results, overall zinc appears to be beneficial under certain circumstances. Several studies are described below in which zinc is administered as a lozenge or zinc-containing syrup that temporarily "sticks" in the mouth and throat. This allows zinc to make contact with the rhinovirus in those areas.

In a randomized, double-blind, placebo-controlled clinical trial, 50 subjects (within 24 hours of developing the common cold) took a zinc acetate lozenge (13.3 mg zinc) or placebo every 2–3 wakeful hours. Compared with placebo, the zinc lozenges significantly reduced the duration of cold symptoms (cough, nasal discharge, and muscle aches) [67].

In another clinical trial involving 273 participants with experimentally induced colds, zinc gluconate lozenges (providing 13.3 mg zinc) significantly reduced the duration of illness compared with placebo but had no effect on symptom severity [68]. However, treatment with zinc acetate lozenges (providing 5 or 11.5 mg zinc) had no effect on either cold duration or severity. Neither zinc gluconate nor zinc acetate lozenges affected the duration or severity of cold symptoms in 281 subjects with natural (not experimentally induced) colds in another trial [68].

In 77 participants with natural colds, a combination of zinc gluconate nasal spray and zinc orotate lozenges (37 mg zinc every 2–3 wakeful hours) was also found to have no effect on the number of asymptomatic patients after 7 days of treatment [69].

In September of 2007, Caruso and colleagues published a structured review of the effects of zinc lozenges, nasal sprays, and nasal gels on the common cold [66]. Of the 14 randomized, placebo-controlled studies included, 7 (5 using zinc lozenges, 2 using a nasal gel) showed that the zinc treatment had a beneficial effect and 7 (5 using zinc lozenges, 1 using a nasal spray, and 1 using lozenges and a nasal spray) showed no effect.

More recently, a Cochrane review concluded that "zinc (lozenges or syrup) is beneficial in reducing the duration and severity of the common cold in healthy people, when taken within 24 hours of onset of symptoms" [70]. The author of another review completed in 2004 also concluded that zinc can reduce the duration and severity of cold symptoms [65]. However, more research is needed to determine the optimal dosage, zinc formulation and duration of treatment before a general recommendation for zinc in the treatment of the common cold can be made [70].

As previously noted, the safety of intranasal zinc has been called into question because of numerous reports of anosmia (loss of smell), in some cases long-lasting or permanent, from the use of zinc-containing nasal gels or sprays [14-16].

Age-related macular degeneration

Researchers have suggested that both zinc and antioxidants delay the progression of age-related macular degeneration (AMD) and vision loss, possibly by preventing cellular damage in the retina [71,72]. In a population-based cohort study in the Netherlands, high dietary intake of zinc as well as beta carotene, vitamin C, and vitamin E was associated with reduced risk of AMD in elderly subjects [73]. However, the authors of a systematic review and meta-analysis published in 2007 concluded that zinc is not effective for the primary prevention of early AMD [74], although zinc might reduce the risk of progression to advanced AMD.

The Age-Related Eye Disease Study (AREDS), a large, randomized, placebo-controlled, clinical trial (n = 3,597), evaluated the effect of high doses of selected antioxidants (500 mg vitamin C, 400 IU vitamin E, and 15 mg beta-carotene) with or without zinc (80 mg as zinc oxide) on the development of advanced AMD in older individuals with varying degrees of AMD [72]. Participants also received 2 mg copper to prevent the copper deficiency associated with high zinc intakes. After an average follow-up period of 6.3 years, supplementation with antioxidants plus zinc (but not antioxidants alone) significantly reduced the risk of developing advanced AMD and reduced visual acuity loss. Zinc supplementation alone significantly reduced the risk of developing advanced AMD in subjects at higher risk but not in the total study population. Visual acuity loss was not significantly affected by zinc supplementation alone. A follow-up AREDS2 study confirmed the value of this supplement in reducing the progression of AMD over a median follow-up period of 5 years [75]. Importantly, AREDS2 revealed that a formulation providing 25 mg zinc (about one-third the amount in the original AREDS formulation) provided the same protective effect against developing advanced AMD.

Two other small clinical trials evaluated the effects of supplementation with 200 mg zinc sulfate (providing 45 mg zinc) for 2 years in subjects with drusen or macular degeneration. Zinc supplementation significantly reduced visual acuity loss in one of the studies [76] but

had no effect in the other [77].

A Cochrane review concluded that the evidence supporting the use of antioxidant vitamins and zinc for AMD comes primarily from the AREDS study [71]. Individuals who have or are developing AMD should talk to their health care provider about taking a zinc-containing AREDS supplement.

Interactions with iron and copper

Iron-deficiency anemia is a serious world-wide public health problem. Iron fortification programs have been credited with improving the iron status of millions of women, infants, and children. Fortification of foods with iron does not significantly affect zinc absorption. However, large amounts of supplemental iron (greater than 25 mg) might decrease zinc absorption [2,78]. Taking iron supplements between meals helps decrease its effect on zinc absorption [78].

High zinc intakes can inhibit copper absorption, sometimes producing copper deficiency and associated anemia [79,80]. For this reason, dietary supplement formulations containing high levels of zinc, such as the one used in the AREDS study [72], sometimes contain copper.

Health Risks from Excessive Zinc

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 [2]. One case report cited severe nausea and vomiting within 30 minutes of ingesting 4 g of zinc gluconate (570 mg elemental zinc) [81]. 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 [82]. 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 [2]. The doses of zinc used in the AREDS study (80 mg per day of zinc 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 [83].

The FNB has established ULs for zinc (Table 3). Long-term intakes above the UL increase the risk of adverse health effects [2]. The ULs do not apply to individuals receiving zinc for medical treatment, but such individuals should be under the care of a physician who monitors them for adverse health effects.

Table 3: Tolerable Upper Intake Levels (ULs) for Zinc [2]

Age	Male	Female	Pregnant	Lactating
0–6 months	4 mg	4 mg		
7–12 months	5 mg	5 mg		
1–3 years	7 mg	7 mg		
4–8 years	12 mg	12 mg		
9–13 years	23 mg	23 mg		
14–18 years	34 mg	34 mg	34 mg	34 mg
19+ years	40 mg	40 mg	40 mg	40 mg

Interactions with Medications

Zinc supplements have the potential to interact with several types of medications. A few examples are provided below. Individuals taking these medications on a regular basis should discuss their zinc intakes with their healthcare providers.

Antibiotics

Both quinolone antibiotics (such as Cipro®) and tetracycline antibiotics (such as Achromycin® and Sumycin®) interact with zinc in the gastrointestinal tract, inhibiting the absorption of both zinc and the antibiotic [84,85]. Taking the antibiotic at least 2 hours before or 4–6 hours after taking a zinc supplement minimizes this interaction [86].

Penicillamine

Zinc can reduce the absorption and action of penicillamine, a drug used to treat rheumatoid arthritis [87]. To minimize this interaction, individuals should take zinc supplements at least 2 hours before or after taking penicillamine [85].

Diuretics

Thiazide diuretics such as chlorthalidone (Hygroton®) and hydrochlorothiazide (Esidrix® and HydroDIURIL®) increase urinary zinc excretion by as much as 60% [88]. Prolonged use of thiazide diuretics could deplete zinc tissue levels, so clinicians should monitor zinc status in patients taking these medications.

Zinc and Healthful Diets

The federal government's 2015-2020 *Dietary Guidelines for Americans* notes that "Nutritional needs should be met primarily from foods. … Foods in nutrient-dense forms contain essential vitamins and minerals and also dietary fiber and other naturally occurring substances that may have positive health effects. In some cases, fortified foods and dietary supplements may be useful in providing one or more nutrients that otherwise may be consumed in less-than-recommended amounts."

For more information about building a healthy diet, refer to the *Dietary Guidelines for Americans* and the U.S. Department of Agriculture's MyPlate.

The *Dietary Guidelines for Americans* describes a healthy eating pattern as one that:

- Includes a variety of vegetables, fruits, whole grains, fat-free or low-fat milk and milk products, and oils.
  Whole grains and milk products are good sources of zinc. Many ready-to-eat breakfast cereals are fortified with zinc.
- Includes a variety of protein foods, including seafood, lean meats and poultry, eggs, legumes (beans and peas), nuts, seeds, and soy products.
  Oysters, red meat, and poultry are excellent sources of zinc. Baked beans, chickpeas, and nuts (such as cashews and almonds) also contain zinc.
- Limits saturated and *trans* fats, added sugars, and sodium.
- Stays within your daily calorie needs.

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