



Copper

Fact Sheet for Health Professionals

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Introduction

Copper, an essential trace element, is available in the diet as a dietary supplement and in food. It functions as a dietary supplement in the activation of cuproenzymes involved in iron metabolism and angiogenesis; it is also important for brain development. In addition, deferiprone, a drug containing superoxide dismutase [1,2].



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A wide variety of plant and animal foods contain copper, and the average human diet provides approximately 1,400 mcg/day for men and 1,100 mcg/day for women that is primarily absorbed in the upper small intestine [1,2,7-9]. Almost two-thirds of the body's copper is located in the skeleton and muscle [1,3].

Only small amounts of copper are typically stored in the body, and the average adult has a total body content of 50–120 mg copper [1,2]. Most copper is excreted in bile, and a small amount is excreted in urine. Total fecal losses of copper of biliary origin and nonabsorbed dietary copper are about 1 mg/day [1,2]. Copper levels in the body are homeostatically maintained by copper

absorption from the intestine and copper release by the liver into bile to provide protection from copper deficiency and toxicity [3].

Copper status is not routinely assessed in clinical practice, and no biomarkers that accurately and reliably assess copper status have been identified [2]. Human studies typically measure copper and cuproenzyme activity in plasma and blood cells because individuals with known copper deficiency often have low blood levels of copper and CP [2]. However, plasma CP and copper levels can be influenced by other factors, such as estrogen status, pregnancy, infection, inflammation, and some cancers [2]. Normal serum concentrations are 10–25 μmol/L (63.5–158.9 mcg/dL) for copper and 180–400 mg/L for CP [10].

Recommended Intakes

Intake recommendations are developed by the Dietary Reference Intakes (DRI) Committee in the National Research Council Board on Medicine [3]. DRI values are used to assess nutrient intakes of groups of people and sex, and include the following:

- Recommended Daily Allowance (RDA): sufficient intake for nearly all healthy individual
- Adequate Intake (AI): adequate intake estimated to meet the requirements of 97%–98% of healthy individuals
- Estimated Average Intake (EAI): estimated to meet the requirements of 50% of healthy individuals; usually used to assess the nutrient intakes of groups of people and to plan nutritionally adequate diets for them; can also be used to assess the nutrient intakes of individuals
- Tolerable Upper Intake Level (UL): Maximum daily intake unlikely to cause adverse health effects

Table 1 lists the current RDAs for copper [3]. For infants from birth to 12 months, the FNB established an AI for copper that is equivalent to the mean intake of copper in healthy, breastfed infants.

Table 1: Recommended Dietary Allowances (RDAs) for Copper [3]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months*	200 mcg	200 mcg		
7–12 months*	220 mcg	220 mcg		
1–3 years	340 mcg	340 mcg		
4–8 years	440 mcg	440 mcg		
9–13 years	700 mcg	700 mcg		
14–18 years	890 mcg	890 mcg	1,000 mcg	1,300 mcg
19+ years	900 mcg	900 mcg	1,000 mcg	1,300 mcg

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*Adequate Intake (AI)

Sources of Copper

Food

The richest dietary sources of copper are organ meats, wheat bran, and whole grains. Copper absorption of copper from plant foods is lower than from animal foods because copper bioavailability is lower in plants [2]. The recommended intake of copper in the diet; however, is based on the amount of copper that contains only about 400 mcg/day.

Tap water and drinking water contain varying amounts of copper. In the United States, the concentration of copper in tap water ranges from 0.0005 mg/L to 1 mg/L [2,11].

Several food sources of copper are noted in Table 2.



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Table 2: Copper Content of Selected Foods [12]

Food	Micrograms (mcg) per serving	Percent DV*
Beef, liver, pan fried (3 ounces)	12,400	1,378
Oysters, eastern, wild, cooked, 3 ounces	4,850	539
Baking chocolate, unsweetened, 1 ounce	938	104
Potatoes, cooked, flesh and skin, 1 medium potato	675	75
Mushrooms, shiitake, cooked, cut pieces, ½ cup	650	72

Food	Micrograms (mcg) per serving	Percent DV*
Cashew nuts, dry roasted, 1 ounce	629	70
Crab, Dungeness, cooked, 3 ounces	624	69
Sunflower seed kernels, toasted, ¼ cup	615	68
Turkey, giblets, simmered, 3 ounces	588	65
Chocolate, dark, 70%–85% cacao solids, 1 ounce	501	56
Tofu, raw, firm, ½ cup	476	53
Chickpeas, mature seeds, ½ cup	289	32
Millet, cooked, 1 cup	280	31
Salmon, Atlantic, wild, cooked, 3 ounces	273	30
Pasta, whole wheat, cooked, 1 cup (not packed)	263	29
Avocado, raw,	219	24
Figs, dried, ½ cup	214	24
Spinach, boiled	157	17
Asparagus, cooked	149	17
Sesame seeds	147	16
Turkey, ground	128	14
Cereal, Cream of Wheat, 1 cup	104	12
Tomatoes, raw	53	6
Yogurt, Greek, plain, 1 cup	42	5
Milk, nonfat, 1 cup	27	3
Apples, raw, without skin, 1 medium	17	2



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*DV = Daily Value. The U.S. Food and Drug Administration (FDA) developed DVs to help consumers compare the nutrient contents of foods and dietary supplements within the context of a total diet. The DV for copper is 0.9 mg (900 mcg) for adults and children age 4 years and older [13]. FDA does not require food labels to list copper content unless copper has been added to the food. Foods providing 20% or more of the DV are considered to be high sources of a nutrient, but foods providing lower percentages of the DV also contribute to a healthful diet.

The U.S. Department of Agriculture's (USDA's) [FoodData Central](#) (<https://fdc.nal.usda.gov/>) [12] lists the nutrient content of many foods.

Dietary supplements

Copper is available in dietary supplements containing only copper, in supplements containing copper in combination with other ingredients, and in many multivitamin/mineral products [14]. These supplements contain many different forms of copper, including cupric oxide, cupric sulfate, copper amino acid chelates, and copper gluconate. To date, no studies have compared the bioavailability of copper from these and other forms [15]. The amount of copper in dietary supplements typically ranges from a few micrograms to 15 mg (about 17 times the DV for copper) [14].

Copper Intake

Typical diets in the United States provide intakes of copper that are slightly above the EAR for children aged 2–19 [9]. Mean intakes from food are 1,400 mcg/day, while intakes from dietary supplements are approximately 1,700 mcg/day.

According to a National Health and Nutrition Survey, 10% of children take dietary supplements [16]. In those who take dietary supplements, copper EAR range from 2.2% to 7.2%.



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Mean dietary intake for children aged 2–19 is copper from dietary sources from food ranging from 1,400 to 1,700 mcg/day.

Health and nutrition status of children who do not meet their copper EAR are below the EAR for children aged 2–19.

Copper Deficiency

Copper deficiency is uncommon in humans [2]. Based on studies in animals and humans, the effects of copper deficiency include anemia, hypopigmentation, hypercholesterolemia, connective tissue disorders, osteoporosis and other bone defects, abnormal lipid metabolism, ataxia, and increased risk of infection [1,17,18].

Groups at Risk of Copper Inadequacy

The following groups are most likely to have inadequate copper status.

People with celiac disease

In a study of 200 adults and children with celiac disease, of which 69.9% claimed to maintain a gluten-free diet, 15% had copper deficiency (less than 70 mcg/dL in serum in men and girls younger than 12 years and less than 80 mcg/dL in women older than 12 years and/or CP less than 170 mg/L) as a result of intestinal malabsorption resulting from the intestinal lining alterations associated with celiac disease [19]. In its 2009 clinical guidelines for celiac disease, the American College of Gastroenterology notes that people with celiac disease appear to have an increased risk of copper deficiency and that copper levels normalize within a month of adequate copper supplementation while eating a gluten-free diet [20].

People with



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Menkes disease is caused by ATPase, leading to signs of copper deficiency. The typical manifestations include cognitive developmental delay, subcutaneous hemangiomas, and reduced mortality.

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People taking

High dietary intakes of zinc can interfere with copper absorption, and excessive use of zinc supplements can lead to copper deficiency. Reductions in erythrocyte copper-zinc superoxide dismutase, a marker of copper status, have been reported with even moderately high zinc intakes of approximately 60 mg/day for up to 10 weeks [3]. People who regularly consume high doses of zinc from supplements or use excessive amounts of zinc-containing denture creams can develop copper deficiency because zinc can inhibit copper absorption. This is one reason the FNB established the UL for zinc at 40 mg/day for adults [1,3].

Copper and Health

This section focuses on two diseases in which copper might play a role: cardiovascular disease (CVD) and Alzheimer's disease.

Cardiovascular disease

Copper deficiency leads to changes in blood lipid levels, a risk factor for atherosclerotic CVD [1]. Animal studies have shown that copper deficiency is associated with cardiac abnormalities, possibly because of the resulting decreases in the activity of several cardiac cuproenzymes [1,2].

However, observational studies of the link between copper concentrations and CVD have had mixed results. A representative cohort study of 1,197

asymptomatic individuals found no association between self-reported copper intakes and serum total cholesterol or low-density lipoprotein [LDL] cholesterol levels. In contrast, another study found that LDL cholesterol levels were higher in participants with serum copper concentrations less than 106 mcg/dL compared to those with concentrations greater than 106 mcg/dL.

In a study of 19,000 men and women, it was found that the risk of developing coronary heart disease was higher among participants aged 40 years and older with serum copper concentrations less than 106 mcg/dL compared to those with concentrations greater than 106 mcg/dL. In addition, the risk of developing coronary syndrome was higher among participants with serum copper concentrations less than 106 mcg/dL compared to those with concentrations greater than 106 mcg/dL. In the 30% who had the lowest serum copper concentrations, the hazard ratio for death from CVD was 1.58 for copper and 3.02 for CP concentrations in serum—

for death from CVD in the highest (mean 147 mcg/dL for copper, 38.3 mg/dL for CP) versus the lowest (81.6 mcg/dL for copper, 22.9 mg/dL for CP) quartiles [26].

A few small studies that assessed the impact of copper supplementation in healthy adults have found little evidence that supplementation affects CVD risk factors. For example, daily supplementation with 2 mg copper as copper glycinate for 8 weeks in 70 healthy adults age 45 to 60 years increased the activity of two cuproenzymes, erythrocyte superoxide dismutase 1 and plasma CP, but had no effect on five other CVD-related plasma markers (CRP,



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homocysteine, total cholesterol, high-density lipoprotein cholesterol, and LDL cholesterol) [27]. In 16 healthy women (mean age 24 years), daily supplementation with 3 mg or 6 mg elemental copper as copper sulfate had no significant effect on CVD risk factors, including total plasma cholesterol or triacylglycerol concentrations [28]. However, the concentration of fibrinolytic factor PAI-I decreased by about 30% (indicating reduced CVD risk) with 6 mg/day copper supplementation compared with placebo. No clinical trials of copper supplementation have been conducted in people with increased CVD risk.

Overall, the evidence to date is insufficient to support any conclusions about the association between copper concentrations and CVD risk or the impact of copper supplementation on CVD.

Alzheimer's disease

Some experts and pathophysiology because of se dependent enzymes. evidence shows Alzheimer's disease the brains of patients excess amounts of disease [31]. For Alzheimer's disease, copper intakes



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A few observational studies have examined dietary copper levels and Alzheimer's disease, with mixed results. One study, for example, assessed cognitive function using four cognitive tests during home visits every 3 years for 6 years and intakes of copper and saturated and trans fats using a food frequency questionnaire in 3,718 community-dwelling (noninstitutionalized) adults age 65 and older [33]. In the overall study population, dietary and total copper intakes were not associated with cognitive decline. However, in 604 participants (16.2%) who consumed a diet higher in saturated and trans fat, total copper intake in the highest quintile (median 2.75 mg/day) was associated with a significantly faster rate of cognitive decline compared with the lowest intake quintile (median 0.88 mg/day). In contrast, an

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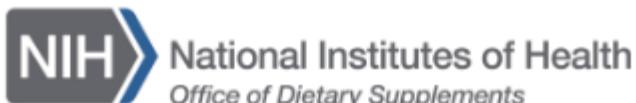
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analysis of data on 1,112 adults older than 60 years found no differences in serum copper or CP levels between patients with Alzheimer's disease (n=211) and healthy controls (n=695) [32]. This study did reveal, however, a significant decline in serum copper not bound to CP in patients with mild cognitive impairment or Alzheimer's disease compared with the healthy control group 18 months after baseline.

Meta-analyses have found that people with Alzheimer's disease tend to have higher serum copper levels than adults without the disease. In a meta-analysis of 10 studies in 867 healthy individuals and 599 with Alzheimer's disease (mean age greater than 70 years in both groups), patients with Alzheimer's disease had significantly higher serum levels of copper not bound to CP and total serum copper than healthy controls [34]. In an earlier meta-analysis of 26 studies in a total of 1,058 patients with Alzheimer's disease and 932 controls + those with Alzheimer's disease and 932 healthy controls



Very little clinical research has been conducted on the effects of copper supplementation in patients with Alzheimer's disease. In a study of patients age 50–70 years with mild cognitive impairment who were randomly assigned 68 mg copper daily or a placebo, there was no difference in cognitive function between the two groups.

Experts participating in a recent meeting of the NIH Alzheimer's Disease and Parkinson's Disease Treatment Efficacy Review Group suggested that copper may play a role in Alzheimer's disease risk. Brain tissue from Alzheimer's disease patients contains higher levels of copper than normal brain tissue. Copper may contribute to the progression of Alzheimer's disease because excess copper can damage brain cells. In some patients with Alzheimer's disease, copper levels in the blood are higher than in some patients without the disease.

whether high or low levels of serum or plasma copper are associated with Alzheimer's disease risk and whether supplements containing copper could affect Alzheimer's disease risk or symptoms.

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Health Risks from Excessive Copper

Chronic exposure to high levels of copper can result in liver damage and gastrointestinal symptoms (e.g., abdominal pain, cramps, nausea, diarrhea, and vomiting) [10,38]. Copper toxicity is rare in healthy individuals who do not have a hereditary copper homeostasis defect. However, copper toxicity has been

reported in people who consume water containing high levels of copper as a result of stagnant water in copper-containing pipes and fixtures as well as copper alloys in water distribution systems and household plumbing that allow copper to leach into water [10,38]. The Environmental Protection Agency has established a recommended upper limit for copper in public water systems of 1.3 mg/L [38,39].

People with Wilson's disease, a rare, autosomal recessive disease, have a high risk of copper toxicity. Wilson's disease, which is caused by a mutation in *ATP7B*, leads to abnormally high tissue levels of copper as a result of defective copper clearance [40]. People with this disease can develop neurologic and liver damage that can result in cirrhosis [1]. Patients can also develop acute hepatitis, hemolytic crisis, and liver failure. Lifelong copper chelation therapy or high doses of zinc can prevent permanent organ damage in these patients.

The FNB has established Tolerable Upper Intake Levels (ULs) for healthy individuals based on the best available scientific information. These ULs do not apply to individuals with specific medical conditions or under medical supervision.



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Table 3: Tolerable Upper Intake Levels (ULs)

Age	Infant Formula	Breast Milk	Lactation
Birth to 6 months	500 mcg	500 mcg	
7–12 months	3,000 mcg	3,000 mcg	
1–3 years	5,000 mcg	5,000 mcg	
4–8 years	5,000 mcg	5,000 mcg	
9–13 years	5,000 mcg	5,000 mcg	
14–18 years	8,000 mcg	8,000 mcg	8,000 mcg
19+ years	10,000 mcg	10,000 mcg	10,000 mcg

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* Breast milk, formula, and food should be the only sources of copper for infants.

Interactions with Copper

Copper is not known to have any clinically relevant interactions with medications.

Copper and Healthful Diets

The federal government's 2020–2025 *Dietary Guidelines for Americans* notes that "Because foods provide an array of nutrients and other components that have benefits for health, nutritional needs should be met primarily through foods. ... In some cases, fortified foods and dietary supplements are useful when it is not possible otherwise to meet needs for one or more nutrients (e.g., during specific life stages such as pregnancy)."

For more information about building a healthy dietary pattern, refer to the *Dietary Guidelines for Americans* (<https://www.dietaryguidelines.gov>) and the USDA's *MyPlate*. (<https://www.myplate.gov>)

The *Dietary Guidelines* note that



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- Includes a variety of fruits and vegetables; whole grains; low-fat dairy products; lean protein sources (such as fish, poultry, and beans); and healthy fats (such as olive oil).
- Includes a variety of whole grains; low-fat dairy products; lean protein sources (such as fish, poultry, and beans); and healthy fats (such as olive oil).
- Limits foods high in solid fats, added sugars, and sodium.
- Limits alcoholic beverages.
- Stays within your daily calorie needs.

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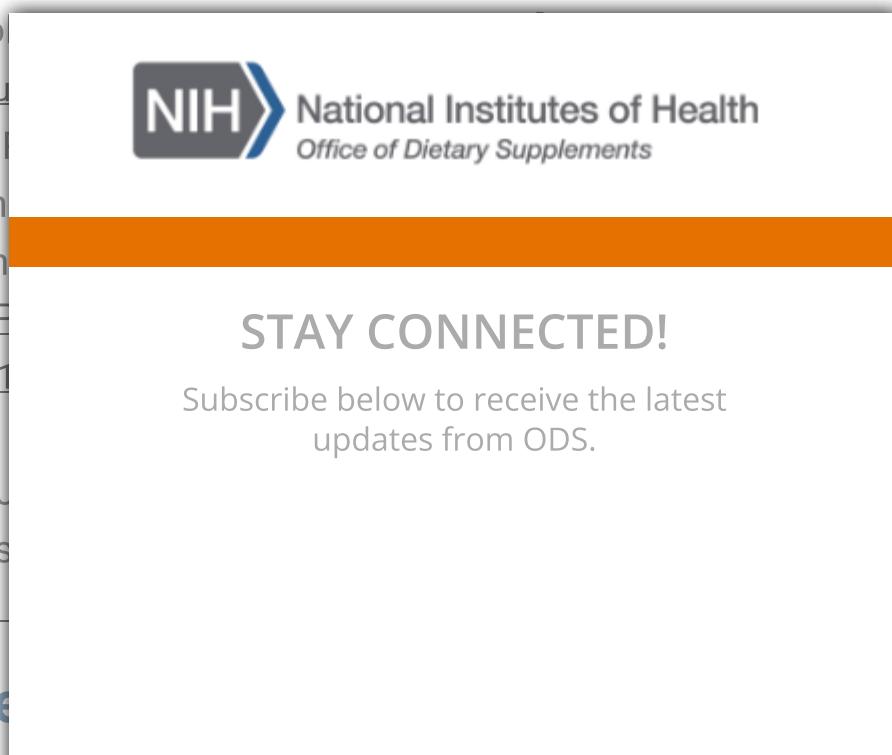
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