REVIEW ARTICLE

Therapeutic Use of Trace Elements in Dermatology

Anita Gade, DO; Jacqueline R. Hwang, BS; Karl Hoegler, MD; Samiya Khan, BS; Amor Khachemoune, MD, FAAD, FACMS

ABSTRACT

Trace elements (microminerals) play a role in many physiological functions, including hormone production and cellular growth. However, their importance in diagnosing and treating dermatologic disease has not been well examined. In this review, we discuss the functions, sources, and recommended requirements of each micromineral. In addition, we analyze the systemic and dermatologic manifestations associated with micromineral imbalances. The pathogenesis of genodermatoses, such as Wilson disease, Menkes disease, acrodermatitis enteropathica, and allergic dermatitis, are also discussed. Included are studies examining the potential therapeutic role of zinc, selenium, and copper in inflammatory diseases, skin cancer, and photoaging. (*Altern Ther Health Med.* 2023;29(4):246-252).

Anita Gade, DO; New York Institute of Technology College of Osteopathic Medicine, Old Westbury, NY, USA. **Jacqueline R. Hwang, BS; Karl Hoegler, MD;** University of Maryland School of Medicine, Baltimore, MD, USA. **Samiya Khan, BS;** Long School of Medicine, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA. **Amor Khachemoune MD, FAAD, FACMS;** Long School of Medicine, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA; University of Central Florida College of Medicine, Orlando, FL, USA; Veterans Affairs Medical Center, Brooklyn, NY, USA; SUNY Downstate, Department of Dermatology, Brooklyn, NY, USA.

Corresponding author: Amor Khachemoune, MD, FAAD, FACMS
E-mail: amorkh@gmail.com

INTRODUCTION

While trace elements (microminerals) make up only 0.02% of human body weight, their function is critical for life.[1] It is important to maintain balanced levels of microminerals as both deficiencies and overconsumption have physiological consequences.[2] With this review we hope to inform clinicians about the dermatologic and systemic manifestations associated with each trace element. In addition, we hope to elucidate the role of microminerals as adjuncts in dermatologic treatments. Understanding the deficiencies, toxicities, and therapeutic actions of each micromineral may help in earlier recognition of illness or resolution of existing disease.

Methods

An in-depth search was performed using PubMed, Embase, MEDLINE, Cochrane Reviews, Google Scholar, DeepDyve, and the keywords: *trace element*, *chromium, cobalt*, *copper*, *fluorine*, *iodine*, *iron*, *manganese*, *molybdenum*, *selenium*, *zinc*, *dermatology*, *toxicity*, and *deficiency*. Articles written in English and addressing the metabolism or dermatological role of microminerals were chosen.

Chromium

Chromium is an essential micromineral that exists in two states: (1) trivalent (Cr^{3+}) is biologically active and present in food, and (2) hexavalent (Cr^{6+}) is a toxic product of pollution. Trivalent chromium plays a crucial role in increasing insulin receptor–mediated signaling for the metabolism of carbohydrate, fat, and protein.[3] Although rare, chromium deficiency has been reported in patients receiving long-term intravenous nutrition, leading to symptoms of hyperglycemia, weight loss, and peripheral neuropathy.[4] Thus, chromium is routinely added in total parenteral nutrition.[5] However, supplementation is not indicated for type 2 diabetes control.[6]

Dietary sources of Cr^{3+} include seafood, meat, whole grains, bananas, and black pepper. The recommended daily allowance (RDA) is 30 µg/day, with more needed in pregnant women and hospitalized patients.[7]

Hexavalent chromium is a known trigger of irritant and allergic contact dermatitis.[8] Irritant dermatitis is due to the cytotoxic properties of Cr^{6+}, while allergic contact dermatitis

results from an immune response to its absorption. Patients present with erythematous or vesicular lesions at areas of contact or generalized eczematous dermatitis and swelling.[9] Exposure to chromium-tanned leather constitutes the majority of reported contact allergies.[10-12] New government regulations were approved in Europe to limit Cr^{6+} in leather and cement.[13-15] Systemic contact dermatitis is possible in individuals taking chromium picolinate supplements.[16] Occupational inhalation of chromium may also lead to asthma, dyspnea, tracheobronchitis, and lung cancer.[17,18]

Cobalt

Cobalt was historically used for its brilliant blue pigment in art. In its trivalent form, cobalt participates in the structure of vitamin B12 (cobalamin).[19] B12 serves as a cofactor for methionine synthase and L-methylmalonyl-CoA mutase—which are crucial for nervous system function—and hemoglobin and DNA synthesis.[20] Dietary sources include mushrooms, tofu, meat, eggs, and dairy. Vegetarian and vegan patients are advised to consume cereals fortified with B12 to prevent deficiency. The RDA is 2.4 μg/day.[21] Interestingly, the most common causes of B12 deficiency in the US are not related to diet, but rather malabsorption, pernicious anemia, bariatric surgery, and long-term use of metformin or acid reducers.[22,23]

Vitamin B12 deficiency manifests dermatologically as hyperpigmentation (due to increased angiogenesis and melanin production in the basal layer of the epidermis), glossitis, linear nail streaks, and poliosis.[24-26] While rare, there have also been reports of vitiligo in B12-deficient patients.[27] As a therapeutic, topical cobalamin is an effective treatment for atopic dermatitis and psoriasis.[28,29] An in vitro study demonstrated that B12 suppresses cytokine, which may explain its immunomodulatory effects in atopic dermatitis.[30] Nonetheless, cases of acneiform eruptions, rosacea, and dermatitis have been reported following B12 therapy.[25]

In some patients, excess consumption of cobalt has been shown to trigger dyshidrotic eczema, necessitating the adoption of low-cobalt diets for these patients.[31] Overall, animal feed, metal objects, occupational exposure (paints, glass, cement), medical implants, and cosmetics are the most common sources of cobalt-related allergic contact dermatitis.[32-34] Systemic cobalt toxicity may manifest as cardiomyopathy due to mitochondrial damage from heavy metal oxidative phosphorylation, or thyroid, liver, neuro-ocular, and bone marrow dysfunction associated with cobalt–chromium joint replacements.[35,36] In the US, patients with an orthopedic implant are observed for symptoms of metal toxicity, such as eczematous dermatitis, joint effusion, swelling, or stiffness.

Copper

Copper functions as a cofactor for enzymes involved in erythrocyte and leukocyte production, iron metabolism, melanin synthesis, cross-linking of elastin and collagen, bone strength, brain development, and the immune system.[37] Sources of copper include shellfish, whole grains, legumes, nuts, and leafy green vegetables. The RDA for adults is 900 μg/day.[7] Oral copper gluconate supplementation may also be used at higher doses (2-8 mg/day) than the RDA for copper deficient patients. These doses are well tolerated and have been shown to improve neuropathy in deficient patients, though more research is needed.[38]

While dietary copper deficiency is rare, Menkes disease and vitiligo can cause low copper levels. Menkes disease is an X-linked disorder of impaired copper absorption due to mutations in the ATP7A gene. Symptoms include sparse kinky hair, low body weight, hypotonia, seizures, and intellectual disability by 3 years of age.[39] A meta-analysis comparing 891 patients with vitiligo and 1682 healthy patients showed that serum copper levels were significantly lower in vitiligo patients compared to healthy controls, though the mechanism is unknown.[40]

On the other hand, Wilson disease is characterized by copper overload due to mutations in the ATP7B gene, leading to a lack of copper excretion in the bile. Patients present with symptoms of skin pigmentation, azure lunulae, hepatitis, renal failure, and brain disorders as early as 4 years of age and as late as the fifth decade of life.[41,42] Standard treatment includes copper chelation (penicillamine and trientine) to promote urinary excretion, or oral zinc, which blocks enterocyte absorption of copper.[43]

GHK-Cu, a copper peptide, is used in cosmetics to promote anti-aging and stimulate collagen, elastin, and glycosaminoglycan synthesis. A 12 week application of facial cream containing GHK-Cu in 71 women with signs of photoaging showed increased skin density, decreased laxity, and reduced depth of wrinkles.[44] Microneedling is a safe and effective way to enhance GHK-Cu delivery into the skin.[45] Treatment of vitiligo with copper cream is an interesting area of speculation, as prior studies have observed abnormally low serum copper levels in patients with vitiligo.[40,46] However, currently there have been no studies investigating this effect.

Data on dermal irritation by copper is limited, although there are a few reports of copper-induced allergic reactions after long-term exposure.[47] One review concludes that copper is a weak sensitizer compared with other metallic compounds.[48]

Fluorine

Fluorine only exists in combination with other elements to create fluoride compounds. Fluoride ions play an important role in tooth mineralization and bone development. Several studies have illustrated that low doses of fluoride salts can be used in postmenopausal patients with osteoporosis to prevent bone loss and fracture.[49] Sources of fluorine include fluoridated tap water, fluoridated toothpaste, seafood, wine, and gelatin. Infants can acquire fluoride through formula, as breast milk lacks significant amounts of fluoride. The Adequate Intake (AI) is 4 mg/day in males and 3 mg/day in females.

Nondietary fluoride toxicity rarely occurs, but can lead to fluorosis characterized by crumbling of the teeth, brittle bones, and ligamentous calcifications. Infants consuming excess fluoride may present with faint white streaks on the teeth.[50]

Dermatologically, excess fluoride has been reported to cause perioral dermatitis, especially with the use of fluoride toothpaste in treating dental cavities.[50,51] However, it is recommended that fluoride toothpaste use should not be stopped, as the benefits outweigh the potential adverse reaction.[51,52] Instead, medical and dental professionals should aim to develop better methods to administer fluoride for oral health, while limiting side effects.

While fluoridation is the addition of a negatively charged fluoride ion to a compound, fluorination is the addition of a neutral fluorine atom. Many topical corticosteroids contain a fluorine atom at the C6 or C9 position to enhance potency and are thus fluorinated. Both fluorinated and unfluorinated steroids are associated with perioral dermatitis and can lead to skin atrophy and telangiectasias if left untreated.[53]

Iodine

Iodine is crucial for metabolism, growth, and development. It serves as an important component of thyroxine (T_4) and triiodothyronine (T_3) and is stored mainly in the thyroid gland.[54] Iodine can exist as a neutral atom (I), a negative iodide ion (I^-), potassium iodide (KI), or potassium iodate (KIO_3). Dietary iodine is first converted to I^- before it is absorbed in the gastrointestinal tract. Endogenous T_4, however, is absorbed without conversion to I^-. Plasma iodide can be excreted by the kidney or taken up by the thyroid, where it may be converted into thyroid hormone or stored as iodine.[54]

Dietary sources include iodized salt, seaweed, shellfish, dairy, eggs, strawberries, and fortified breads. The RDA is 150 µg/day (more is required in pregnant women).

Iodine deficiency affects approximately 2 billion people worldwide with 50 million people presenting with symptoms.[55] Inadequate iodine intake impairs thyroid hormone synthesis, leading to neurological issues, goiter, slowed metabolism, weight gain, and cold intolerance. Due to higher nutrient demands, fetuses are the most vulnerable to iodine deficiency and may suffer from cretinism, an irreversible form of arrested physical development and intellectual disability.[55] Excess iodine does not generally lead to clinical manifestations, but those with pre-existing thyroid disease, the elderly, and neonates may experience hypothyroidism or hyperthyroidism.[56]

Iodine deficiency manifests dermatologically as brittle nails, dry skin, and hair loss due to thyroid deficiency. One study determined that iodine could be applied to areas of hair loss in pediatric patients suffering from alopecia areata.[57] Potassium iodide (KI) may also be used to treat inflammatory dermatoses and mycoses, although newer drugs have largely replaced its use. Until the approval of itraconazole, saturated solutions of potassium iodide (SSKI) were the standard of treatment for cutaneous sporotrichosis. However, SSKI remains the first choice treatment in resource poor countries due to its lower cost.[55] The antifungal mechanism of KI is still unknown, but its anti-inflammatory properties are due to suppression of neutrophil production of toxic oxygen intermediates.[58] Other dermatological conditions treated with KI include panniculitis and neutrophilic dermatoses, such as pyoderma gangrenosum, Sweet syndrome, and Behcet disease. KI inhibits chemotaxis of neutrophils and synthesis of toxic radicals by polymorphonuclear cells, permitting its use in these diseases.[59]

Iron

Iron is the most abundant micromineral in the body. The body requires iron for the synthesis of hemoglobin and myoglobin, as well as for enzymes involved in oxidation-reduction reactions. Iron is bound and transported in the plasma via transferrin and stored bound to ferritin.[60]

Dietary iron sources include red meats, green leafy vegetables, legumes, and eggs.

The RDA for all age groups of men and postmenopausal women is 8 mg/day; the RDA for premenopausal women is 18 mg/day.[7] Vegetarian and vegan individuals are recommended to consume vitamin C to enhance iron absorption. Iron deficiency is the most common nutritional deficiency worldwide, and is attributed to poor diet, heavy menstruation, blood loss, and inability to absorb iron. Patients with low iron may present with anemia, fatigue, weakness, and dyspnea. The dermatologic manifestations of iron deficiency include pallor, hair loss, brittle nails, and koilonychia (spoon shaped nails).[7]

Various diseases are associated with iron overload. Hereditary hemochromatosis is an autosomal recessive disorder caused by a mutation on the HFE gene, leading to unregulated iron absorption. Affected individuals experience bronze hyperpigmentation on areas of sun-exposed skin.[61] Pathogenesis entails increased melanin synthesis and iron deposits present in skin. If diagnosed early with skin biopsy, patients respond well to phlebotomy treatment, and symptoms may not progress to cirrhosis or cardiomyopathy. Hereditary hemochromatosis may also cause hair loss, ichthyosis, and koilonychia.[61] In addition, high states of iron have been found to elicit blistering skin lesions associated with porphyria cutanea tarda.[62] Sideroblastic anemia is another disorder of iron overload due to the body's inability to synthesize hemoglobin. Patients present with pallor, dyspnea, and splenomegaly.[63] It is also believed that sclerosing panniculitis and leg ulceration associated with chronic venous disease is due to the inflammatory response following extravasation of iron-containing erythrocytes and hemosiderin accumulation in the dermis.[64]

Iron-catalyzed reactive oxygen species generation contributes to cutaneous photodamage. Based on in vitro and mice studies, iron chelators may offer photoprotection, although human trials are needed.[65]

Manganese

Manganese plays a widespread range of physiological roles, including the formation of connective tissue, clotting factors, and sex hormones; metabolism of carbohydrates and lipids; blood sugar regulation; and nervous system function. Manganese supports skin integrity as a cofactor for prolidase,

which is involved in collagen production.[66] It also protects the skin from free radical and ultraviolet (UV) damage by serving as a cofactor for superoxide dismutase (SOD).[66]

Dietary sources include whole grains, pineapples, legumes, nuts, turmeric, and tea. The AI is 2.3 mg/day in males and 1.8 mg/day in females.[7]

Although rare, manganese deficiency is associated with bone demineralization, infertility, seizures, ataxia, and reduced metabolism.[66] One study, in which 7 men were fed a manganese-deficient diet, demonstrated the development of dermatitis with a scaly, erythematous rash.[67] Manganese toxicity, however, leads to poor cognition and neurological conditions resembling Parkinson and Wilson disease.[68]

Interestingly, studies have shown that manganese can be used as an adjunct in wound care. Manganese is essential for the production of proline, which aids in collagen formation and wound healing. While the mechanism is still being investigated, one current theory suggests manganese may upregulate integrin's expression in basal layer keratinocytes.[69] Investigators applied an alginate dressing with manganese and zinc to chronic wounds in 1285 patients for 3 months, which effectively promoted wound healing.[69] In vivo experiments with diabetic mice also revealed accelerated wound healing after manganese superoxide dismutase (MnSOD) gene therapy.[70]

Molybdenum

Molybdenum is a cofactor of sulfite oxidase, aldehyde dehydrogenase, and xanthine oxidase, which catalyze the conversion of sulfite to sulfate, oxidation of purines and pyrimidines, and conversion of xanthine to uric acid, respectively.[71] Dietary sources include dairy, legumes, oats, nuts, and leafy vegetables. The RDA for adults is 45 µg/day.[7]

Molybdenum deficiency is extremely rare, with one case report occurring in a patient with Crohn disease following long-term parenteral nutrition. Symptoms included nausea, tachypnea, tachycardia, vision issues, and coma, but resolved with treatment of ammonium molybdate.[72]

Molybdenum is generally nontoxic to humans. However in Armenia, a region with high concentrations of molybdenum in the soil, excess molybdenum has been associated with painful joints, hyperuricosuria, hallucinations, and seizures.[72]

Since molybdenum and copper exist as physiological opponents, there is elevated urinary copper excretion with larger molybdenum intake. Thus, molybdenum, in the form of ammonium tetrathiomolybdate, is used to treat copper overload in Wilson disease.[73] Unfortunately, there is a lack of literature regarding the therapeutic effects of molybdenum for dermatologic diseases. Therefore, its discussion in dermatology is limited to its role as a possible allergen or in treating copper overload.[74] Further studies are needed to explore the role of molybdenum in skin health.

Selenium

Selenium is an important component of glutathione peroxide and protects against free radicals.[75] Selenium has been shown to protect mice from UV-related skin damage and cancers.[75] Dietary sources include vegetables grown in selenium-rich soil, seafood, meats, grains, and enriched breads. The RDA is 55 µg/day.

Dietary supplementation is recommended to prevent cardiomyopathy, a systemic consequence of selenium deficiency. Selenium deficiency has also been associated with dystrophic epidermolysis bullosa, an autosomal recessive disease that causes fluid-filled blisters, acral skin thickening, loss of fingernails, and atrophic scarring.[76,77] Selenium deficiency has also been commonly reported in psoriasis patients, and the selenium status is related to the severity of the psoriasis.[77] However, supplementation has not been shown to provide therapeutic benefit for psoriasis or in reducing skin cancer risk in humans.[78]

In one case report from Japan, an infant with selenium deficiency presented with dry skin, sparse light hair, and erythema on the face, groin, and extremities that mimicked changes seen with zinc deficiency and responded well to parenteral nutrition.[79] Clinicians should, therefore, be aware of this possible differential diagnosis in infants with xerotic and eczematous skin.[79]

Selenium has one of the narrowest ranges between deficiency(<40 µg/day) and toxicity (>400 µg/day).[80] Selenium toxicity is rare, but can occur after unmonitored consumption of supplements. In 2008, a misformulated supplement containing 200 times the advised selenium concentration led to symptoms of nausea, vomiting, brittle nails, alopecia, irritability, and foul breath in 201 consumers.[80] Patients who consume selenium supplements should therefore be advised to consume this mineral within recommended limits.

Zinc

Zinc is an important cofactor for enzymes involved in gene expression, cell development, collagen synthesis, and immune system function. Zinc is routinely used in dermatologic therapies, including zinc pyrithione shampoo for dandruff and tinea versicolor, and oral zinc sulfate for atopic dermatitis, psoriasis, leishmaniasis, and surgical wound healing.[81] Dietary sources include meat, shellfish, eggs, nuts, legumes, and fortified cereals. The RDA is 11 mg/day in males and 8 mg/day in females.[7]

An estimated 17.3% of the world's population is at risk of zinc deficiency.[82] Risk factors include poor dietary intake, malabsorption, or loss via diuretics or liver disease.[83] Zinc deficiency leads to growth retardation, hypogonadism, hyposmia, lethargy, and delayed wound healing.[84] Moreover, animal studies have associated zinc deficiency with reduced levels of hemoglobin, total erythrocyte count, and packed cell volume in a dose-dependent manner.[85] Dermatologically, zinc deficiency manifests with xerosis, dermatitis, Beau lines on the nail, and alopecia.[86,87]

Zinc deficiency has also been associated with acrodermatitis enteropathica (AE), a rare disorder that impairs zinc absorption from food. Affected children present

with diarrhea, alopecia, muscle wasting, and a vesicular, pustular rash on the extremities and face. Oral zinc sulfate is suggested to greatly help patients with AE.[88] In addition, inadequate zinc impairs wound healing by reducing fibroblast proliferation, collagen synthesis, and epithelialization. Zinc is, therefore, routinely applied to dressings or offered as oral adjuncts to accelerate wound healing.[89] Zinc deficient diets may also elicit acne that is reversed with zinc supplementation.[75] Patients with severe epidermolysis bullosa have also been found to be zinc deficient, and could potentially benefit from supplementation.[90] While individuals with atopic dermatitis have low serum zinc concentrations, supplementation has not been proven effective, and may actually increase pruritic symptoms.[91] Well-designed randomized controlled trials investigating the utility of zinc supplementation in skin disorders is needed.

Acute zinc toxicity causes lethargy, nausea, vomiting, diarrhea, focal neuronal deficits, and an elevated risk of prostate cancer.[84] Dermal exposure to zinc is not a major toxicological risk, although zinc-containing dental fillings can cause systemic contact dermatitis.[92]

The Table shown summarizes the clinical manifestations from the deficiency and toxicity of each micromineral.

Table. Summary of Trace Element Deficiencies, Toxicities, and Therapeutic Use

Trace element	Dietary source	RDA in adults	Function	Effects of deficiency	Causes of toxicity	Effects of toxicity	Therapeutic use
Chromium	Seafood, meat, broccoli, grape juice, potatoes, garlic, yeast, whole grains, green beans, nuts, bananas, egg yolk, black pepper	30 µg/d	Potentiates effects of insulin	**Systemic:** Impaired glucose tolerance	**Systemic:** Excessive supplementation **Dermatologic:** Chromium-tanned leather	**Systemic:** Pulmonary cancer, kidney failure **Dermatologic:** Contact dermatitis, skin ulcers	**Systemic:** Component of parenteral nutrition to prevent diabetes symptoms **Dermatologic:** Need for further human clinical studies
Cobalt	Mushrooms, red meat, fish, tofu, cheese, eggs, B12-fortified cereals	2.5 µg/d	Part of vitamin B12: RBC formation, neurologic function, DNA synthesis	**Systemic:** Not indicated in the literature for cobalt **Dermatologic:** (Vitamin B12): hyperpigmentation, linear nail streaks, poliosis	**Systemic:** Cobalt-chromium joint replacements **Dermatologic:** Animal feed, metal objects, occupational exposure (paints, glass, cement), medical implants, cosmetics	**Systemic:** Cardiomyopathy; neurologic, thyroid, liver problems **Dermatologic:** Allergic contact dermatitis	**Dermatologic**: Need for further human clinical studies
Copper	Shellfish, whole grains, legumes, nuts, potatoes, organ meats, dark leafy green vegetables, dried fruits, cocoa, black pepper, yeast	900 µg/d	Aids in iron metabolism Melanin synthesis, collagen and elastin cross-linking	**Systemic**: Sparse kinky hair, low body weight, hypotonia, seizures, intellectual disability	**Systemic:** Wilson disease	**Systemic:** Skin pigmentation, azure lunulae, hepatitis, renal failure, brain disorder	**Systemic:** Therapy in delaying intellectual symptoms of Menkes disease **Dermatologic:** Potential for copper supplementation in vitiligo patients Copper peptides may be used for anti-aging
Fluorine	Fluoridated water, fluoridated toothpaste, food prepared in fluoridated water, seafood, black tea, wine, potatoes, gelatin, baby formula	4 mg/d in males; 3 mg/d in females	Mineralization for healthy teeth and strong bones	**Systemic:** Dental caries and weak bones	**Systemic:** Fluoridated toothpaste **Dermatologic:** Fluorinated topical steroids	**Systemic:** Fluorosis in adults, white streaks on teeth in infants **Dermatologic:** Perioral dermatitis	**Systemic:** Fluoridated water and toothpaste prevent dental caries, cavities, and decay
Iodine	Iodized salt, seaweed (kelp), scallops, cod, yogurt, shrimp, milk, eggs, strawberries, iodinated bread	150 µg/d	T4 and T3 hormone production Proper fetal development	**Systemic:** Goiter, poor fetal development **Dermatologic:** Brittle nails, dry skin, hair loss		Rare in the US **Systemic**: Thyrotoxicosis and iodine-induced goiter	**Dermatologic:** Topical or oral antifungal treatment for cutaneous sporotrichosis and tinea capitis Topical application for alopecia areata
Iron	Red meat, green leafy vegetables, legumes, eggs	8 mg/d in men and postmenopausal women; 18 mg/d in premenopausal females	Component of hemoglobin and myoglobin, electron carrier in cells, oxygen transport to tissues	**Systemic:** Anemia, fatigue **Dermatologic**: Pallor, brittle nails, hair loss, koilonychia	**Systemic:** Hereditary hemochromatosis	**Dermatologic:** Skin hyperpigmentation	**Dermatologic:** Need for further human clinical studies

Table. (continued)

Manganese	Whole grains (oats, brown rice, bulgur wheat), pineapples, legumes, nuts, turmeric, garlic, tea	2.3 mg/d in males; 1.8 mg/d in females	Collagen production and bone structure Cofactor for SOD enzyme Fat metabolism, blood sugar control, nervous system function	**Systemic**: Impaired skeletal development, infertility, ataxia, convulsions **Dermatologic:** Dermatitis, slowed hair growth		**Systemic:** Parkinsonian-like neurologic symptoms	**Dermatologic:** Wound healing
Molybdenum	Dairy products, legumes, oats, nuts, several green leafy vegetables	75 µg/d	Cofactor of sulfite oxidase, aldehyde dehydrogenase, and xanthine oxidase	**Systemic:** Nausea, tachypnea, tachycardia, vision issues, coma		**Systemic:** Need for further human clinical studies	**Systemic:** Wilson disease **Dermatologic:** Further clinical studies needed
Selenium	Vegetables grown in selenium-rich soil, fish, shellfish, organ meats, grains, nuts, eggs, poultry, garlic, enriched breads	55 µg/d	Antioxidant, immune function, chemopreventive	**Systemic:** Cardiomyopathy **Dermatologic:** Psoriasis, epidermolysis bullosa	Excessive supplementation (toxicity is rare)	**Systemic:** Fatigue, nausea, garlic odor to breath, vomiting **Dermatologic:** Dermatitis, alopecia, brittle nails	**Systemic:** Prevention of cardiomyopathy **Dermatologic:** Epidermolysis bullosa
Zinc	Red meat, poultry, shellfish, eggs, nuts, legumes, fortified cereals	11 mg/d in males; 8 mg/d in females	**Systemic**: DNA synthesis, immune function, metabolism **Dermatologic**: Wound healing, skin membrane integrity	**Systemic:** Gonadal atrophy, anosmia, impaired immunity, anorexia, diarrhea, anemia, lethargy **Dermatologic:** Acrodermatitis enteropathica-like symptoms, acne, xerosis, seborrheic dermatitis, dermatitis, Beau lines, alopecia	Excessive supplementation (toxicity is rare)	**Systemic:** Headaches, nausea, vomiting, diarrhea, fever, anemia	**Dermatologic:** Dandruff, tinea versicolor, wound healing, epidermolysis bullosa, leishmaniasis, psoriasis

Abbreviations: RDA, recommended daily allowance; RBC, red blood cell; SOD, superoxide dismutase.

CONCLUSION

In summary, microminerals play an important role in nutrition and health. Physicians should be aware that inadequate or excess consumption may manifest as systemic and dermatologic disease. In particular, we note the association with contact dermatitis, Menkes disease, vitiligo, alopecia, sporotrichosis, psoriasis, epidermolysis bullosa, acne, atopic dermatitis, acrodermatitis enteropathica, wound healing, and various hair and nail disorders. Additional human clinical trials are needed to assess their full clinical utility as topical and oral adjuvants.

CONFLICT OF INTEREST DISCLOSURES

The authors have no conflicts of interest to disclose.

FUNDING/SUPPORT

The authors have no funding sources to report.

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