International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

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ARTICLE TITLE	ZINC AND HUMAN HEALTH: A REVIEW
ARTICLE INFO	Monika Klimczak, Aleksandra Woskowska, Anna Hanslik, Magdalena Mendak, Agata Białek, Magdalena Domisiewicz. (2025) Zinc and Human Health: A Review. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.3542
DOI	https://doi.org/10.31435/ijitss.3(47).2025.3542
RECEIVED	05 July 2025
ACCEPTED	08 August 2025
PUBLISHED	13 August 2025
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ZINC AND HUMAN HEALTH: A REVIEW

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ABSTRACT

Zinc is one of the micronutrients necessary for the proper functioning of the body. It plays a significant role in many physiological processes. Its concentration should be closely monitored in the body, as both excess and deficiency have health consequences. It occurs in all tissues. Due to its properties, it is currently being used more and more frequently in cosmetology and dermatology.

Aim of study and materials: A comprehensive literature review was conducted using the PubMed and GoogleScholar databases, focusing on articles published since 2020. The search included the keywords: zinc, health, zinc oxide, skin, cosmetology.

Conclusion: After analyzing the current literature, it can be seen how important it is for health to have the right amount of zinc in the body. Zinc is one of the micronutrients necessary for the proper functioning of the body. It is essential for proper metabolism at the cellular level, and it is also a part of many enzyme systems, affecting the digestive, hormonal, and immune systems. However, too much zinc in the body is not neutral for our health. Zinc is also increasingly used in dermatology, cosmetology, and wound treatment. Further research should be conducted to allow for even greater use of zinc properties.

KEYWORDS

Zinc, Health, Zinc Oxide, Skin, Cosmetology

CITATION

Monika Klimczak, Aleksandra Woskowska, Anna Hanslik, Magdalena Mendak, Agata Białek, Magdalena Domisiewicz. (2025) Zinc and Human Health: A Review. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.3542

Introduction.

Zinc is one of the essential micronutrients for humans. In an adult human body, there are 2 to 3 g of zinc, 85% of which is found in muscles and bones, 11% in the skin and liver, and the rest in other tissues [1]. It is a cofactor for over 300 different enzymes and has a regulatory role - it affects the synthesis of proteins, hormones, and red blood cells; the proper functioning of the skin and mucous membranes; and participates in the metabolism of proteins, fats, carbohydrates, and nucleic acids. It plays a significant role in biochemical pathways and cellular functions, such as response to oxidative stress, homeostasis, immune reactions, DNA replication, DNA damage repair, cell cycle progression, and apoptosis.

It is essential for proper metabolism at the cellular level and is also a part of many enzyme systems. The richest sources of zinc are oysters, liver, and egg yolks. Zinc is also found in plant products, such as pumpkin seeds, sesame, linseed oil, and sunflower, but due to the presence of phytates in these products, zinc absorption from them is lower. It is mainly delivered to the body through the digestive system, with food. Zinc is mainly absorbed in the small intestine. The body does not store zinc. The protein ZIP4 [22] is responsible for the absorption of zinc from the intestines. It is most often impaired in gastrointestinal diseases associated with impaired intestinal absorption. Zinc absorption can also be limited by a lack of animal protein, high calcium and iron intake, phytates in plant products, and increased blood sugar levels.

Zinc absorption disorders are observed in almost 17% of the world's population and affect many organ systems, leading to disorders of both humoral and cellular immune response, which increases susceptibility to infections. Zinc in the body is bound to proteins (mainly albumin). That's why its absorption can be impaired in liver diseases. The level of albumin in the body may decrease, which leads to reduced zinc absorption. Inflammatory bowel diseases can also lead to reduced zinc absorption. However, some medications, such as diuretics, can increase its excretion from the body. Symptoms of zinc deficiency are very nonspecific – from mental disorders to frequent infections, immune system disorders, and growth retardation.

The impact of zinc on the immune system

Zinc is involved in the process of prostaglandin formation, which affects the secretory activity of the skin. Its deficiency reduces the activity of the immune system, which can cause dermatoses and allergies. Zinc deficiency changes immune pathways and protein expression patterns, leading to abnormal and impaired immune functions. The development and maturation of T-lymphocytes is also highly dependent on zinc. Zinc deficiency causes an increased Th2 lymphocyte response, leading to increased eosinophilia and the release of pro-inflammatory cytokines and prostaglandin E2, which is why zinc levels may have a significant impact on the development of allergies. Zinc supplementation inhibits the degranulation of mast cells, which reduces histamine production. [10] It was also noted that children who are fed artificially have limited zinc absorption compared to children who are fed naturally with mother's milk, where absorption is higher, which also translates to the occurrence of allergies [10]. Low levels of zinc in the blood may also be considered a risk factor for the development of asthma and allergic rhinitis in children [15].

The effect of zinc on the digestive system

Zinc also significantly affects the proper functioning of the gastrointestinal tract. It is responsible for better regeneration of the intestinal epithelium and better absorption of water and electrolytes, which can contribute to limiting the occurrence of diarrhea. Zinc plays a significant role in maintaining the integrity of the stomach lining. It also has an antimicrobial effect on pathogenic intestinal bacteria - Salmonella and Shigella.

Zinc's role in maintaining intestinal homeostasis is also being increasingly emphasized. A lower concentration of zinc is observed in people with Crohn's disease [20]. Zinc deficiency affects the lowering of epithelial barrier function. To support the intestinal barrier, zinc is used in the form of zinc carnosine. It is an artificially produced derivative of carnosine and zinc, which are combined in a 1:1 ratio [20]. Zinc deficiencies can also increase the risk of gastrointestinal infections. Zinc has also been shown to be effective in treating diarrhea [20]. Zinc supplementation can therefore affect the functions of the intestinal barrier and thus have a beneficial effect on the course of certain diseases.

Zinc Finger Motif

The zinc finger motif is also described in literature. Zinc fingers play a significant role in the recognition and transcription of DNA. Zinc ions are responsible for the stability of the domain. The zinc finger motif allows for the recognition of a specific DNA sequence and the binding of a particular nuclease to unique sequences in the genome. They allow for the binding of specific DNA proteins, for example transcription factors, which are necessary for the proper functioning of cells, their differentiation, growth, and maintenance of many organs [12].

The effect of zinc on the endocrine system

Zinc also plays a role in the hormonal system. Zinc provides structural stability to the insulin molecule. That is why we can observe higher concentrations of zinc in the beta cells of the pancreas than in other cells of the body. It stimulates lipogenesis and glucose uptake into adipocytes by acting on the insulin signaling pathway. The zinc transporter also participates in signaling between the pancreas and the liver. Zinc also plays a significant role in the functioning of thyroid hormones. Regulates the synthesis of TRH, thyrotropin-releasing hormone, and TSH (thyroid-stimulating hormone). Zinc regulates transcription factors necessary for the synthesis of thyroid hormones [13, 25].

Zinc supplementation is important in the case of Hashimoto's disease. Zinc may lower the concentration of antithyroid antibodies due to its antioxidant effect [13, 24]. It participates in the synthesis of thyroxine and the binding of triiodothyronine. Research shows that zinc deficiency significantly increases the titer of antibodies against thyroid peroxidase (anti-TPO). Zinc supplementation can greatly improve the condition of hair, skin, and nails in hypothyroidism.

A connection between Zn levels in serum and glucose and HbA1c levels was also observed. The glucose and HbA1c levels are dependent on the serum zinc level. Too low levels of zinc in the blood cause an increase in glucose and HbA1c levels [14]. I see this in both diabetic and non-diabetic patients.

It is an inhibitor of the 5-alpha-reductase enzyme, which catalyzes the conversion of testosterone to 5α-dihydrotestosterone (DHT). It is therefore responsible for regulating hormonal balance. Dihydrotestosterone is a metabolite of testosterone. Too much testosterone causes overproduction of sebum, hirsutism, and androgenic alopecia. Zinc inhibits the activity of the type 1 and 2 5-α-reductase enzyme, which is why it has anti-androgenic effects. It therefore inhibits overproduction of sebum, hirsutism, and androgenic alopecia [19].

The effect of zinc on male fertility

Large amounts of zinc are found in semen. Zinc is essential for the proper course of spermatogenesis, testicular development, and the structure and quantity of sperm. Zinc deficiency can lead to lower testosterone levels, lower sperm count, and lower sperm viability, which can cause fertility problems.

The conversion of testosterone to its active form, dihydrotestosterone, requires the zinc-dependent 5-alpha reductase [27]. Therefore, zinc plays an important role in testosterone synthesis.

Zinc and senile dementia

Zn(II) ions are part of metalloenzymes directly related to the neurological system. Zn(II) ions are responsible for the release of neurotransmitters into the synaptic cleft. There are studies suggesting that excess zinc is responsible for the symptoms of senile dementia. In cases of cerebral ischemia, glutamate and Zn ions are released from neurons into the synaptic cleft. Excess zinc ions are neurotoxic - they inhibit the work of many enzymes and cellular respiration. Negative effects of zinc combined with an excess of calcium ions cause the death of neurons [26].

Zinc and the risk of cardiovascular disease

The main features of atherosclerosis are chronic inflammation and oxidative stress. The anti-inflammatory properties of zinc may explain its protective effect on blood vessels [28]. The anti-inflammatory and antioxidant properties of zinc may be significant for patients with risk factors for cardiovascular disease. Zinc supplementation reduces the secretion of pro-inflammatory cytokines, which can significantly affect the process of atherosclerosis.

Zinc in cosmetology and its effect on the skin

It is estimated that about 6% of zinc is found in human skin. Most of it is found in the stratum corneum, and its concentration decreases in the deeper layers of the skin. The popularity of zinc in cosmetics is due to the many functions of this ingredient. Zinc is necessary for collagen and white blood cell synthesis, contributes to maintaining healthy skin, and plays a significant role in wound healing.

Zinc oxide (ZnO) is the most commonly used in cosmetology, and it is used in the form of finely divided dust. It has a positive effect on the skin and does not clog pores or irritate the skin. Zinc hydroxide Zn(OH)2 is also used, for example, in the form of a gel, and zinc chloride (ZnCl2) aqueous solutions - these compounds are part of tonics, deodorants, or skin care cosmetics.

Zinc oxide is one of the ingredients commonly used in wound treatment. The antimicrobial mechanism of ZnO is not entirely clear, but it is mainly attributed to the production of reactive oxygen species (ROS) and the release of Zn2+ ions. Zn2+ ions increase the proliferation of fibroblasts and endothelial cells, which further facilitates wound healing and skin regeneration [17].

Zinc supplementation is used to support the treatment of chronic wounds. Zinc is a cofactor for many enzymatic reactions, which is why it is essential for all proliferating cells. The correct concentration of zinc in the blood inhibits the inflammatory process. It is also worth noting that in the case of large wound and ulcer areas, increased proliferative activity in the wound increases the demand for nutrients [22].

Zinc oxide (ZnO) is a component used in barrier creams for the treatment of diaper dermatitis in children and adults. Diaper rash is an acute inflammatory reaction that occurs in newborns and infants, but also in older people who suffer from incontinence. The pathophysiology of diaper dermatitis is multifactorial. Both prolonged skin contact with urine and feces, causing irritation and the development of bacterial enzymes, and increased humidity, which promotes the growth of bacterial strains, have an impact. Zinc oxide limits the growth of bacteria and the inflammatory reaction of the skin due to its antiseptic and anti-inflammatory properties [2].

Zinc oxide is also used in sunscreens to create opaque, inorganic sunscreens. ZnO as a physical UV blocker provides excellent protection against UVA and UVB radiation. Nanoparticles, typically below 100 nm, are used, which, due to their small size, provide effective protection against UV radiation without noticeable residue on the skin [3,16]. The stabilizing properties of zinc ensure the stability of the preparation, thereby allowing it to remain on the skin longer without changing its properties.

Zinc pyrithione (ZnPT) is a popular ingredient in shampoos used to treat dandruff or seborrheic dermatitis. It is currently the most popular anti-dandruff ingredient. Pityriasis versicolor is most often caused by the yeast-like fungus Malassezia, most often Malassezia furfur. Research has shown that ZnPT inhibits the transport of nutrients across the membrane, which are necessary for yeast growth, by inducing membrane depolarization [1]. Research also suggests that ZnPT impairs the ability of fungal cells to assimilate and metabolize nutrients, which leads to the inhibition of Malassezia furfur growth [1]. ZnPT also has properties that make its molecule highly permeable after application to the skin, but at the same time it deposits on the skin, especially in lipid-rich regions, such as the scalp. During the gradual dissolution of ZnPT particles, a structural analog of the natural antibiotic aspergillic acid with antifungal activity against Malassezia is gradually released [1].

The effect of zinc on acne treatment

Zinc is also used in acne therapy. The pathogenesis of acne is very complex. It is caused by excessive production of free radicals, which are generated by factors such as UV radiation, environmental pollution, an unhealthy diet, or stress. Free radicals cause cell damage by interacting with lipids, proteins, and DNA, which causes skin inflammation. The cause of acne is also excessive keratinization of hair follicles and sebaceous gland ducts, increased sebum production leading to blocked pores, and hypoxia in the skin microenvironment, as well as bacterial colonization and proliferation. Due to its anti-inflammatory and antibacterial properties, it is widely used in topical acne therapy. Zinc sulfate is most commonly used. Some studies also suggest that the use of zinc preparations can lead to a decrease in sebum production, which promotes the formation of acne. Zinc oxide also has the ability to inhibit the growth of bacteria, such as Staphylococcus aureus, which are responsible for the formation of acne. Inhibiting bacterial growth is particularly important in the context of growing antibiotic resistance, as these bacteria do not develop resistance to the mechanisms of action of ZnO [8]. ZnO is therefore a good alternative for treating acne instead of commonly used antibiotics, such as tetracycline. Acne is also caused by Cutibacterium acnes bacteria. Zinc oxide nanoparticles stabilized with hyaluronic acid are used, which selectively kill C. acnes while preserving the skin microbiome [9]. HA-ZnO (hyaluronic acid-stabilized zinc oxide nanoparticles) reduce sebum, prevent acne recurrence, and reduce the

risk of scarring. Excessive keratinization of acne skin limits the absorption and penetration of medications. HA-ZnO particles accumulate in the sebaceous glands of the skin, facilitating the penetration of drugs into the deeper layers of the skin. They also show high selectivity towards C. acnes, which means they do not disrupt the natural skin microbiome.

Zinc is used in acne treatment not only for topical treatment but also as oral supplementation. Due to its anti-inflammatory, antibacterial, and anti-androgenic properties, oral zinc is used in combination with low doses of isotretinoin for patients with acne rosacea. Zinc is necessary for the synthesis and release of retinol-binding protein, which transports vitamin A from the liver to target tissues [5]. It has a much better safety profile and fewer side effects than retinoids and can affect the absorption, transport, and utilization of vitamin A [4]. Thanks to this, we can use smaller doses of isotretinoin, which will not only reduce the number of side effects in patients but also reduce the cost of therapy. The margin of safety for oral zinc use is very large – the lethal dose is 27 g/day. Taking too much zinc can cause nausea, vomiting, or copper deficiency [6]. Excessive zinc intake can inhibit the absorption of copper and iron, leading to copper deficiency and anemia, respectively.

Zinc is also used in the external treatment of seborrheic dermatitis, eczema, pustular erosive dermatitis, and wounds of various etiologies. These diseases are accompanied by itching, and zinc is used here due to its soothing properties. Most commonly used are zinc oxide and zinc carbonate preparations [19].

Zinc and atopic dermatitis

Research shows that people with atopic dermatitis have lower levels of zinc. AZS is a chronic inflammatory skin disease. One of the main physiological markers of atopic dermatitis is physiological stress. Zinc is a component of superoxide dismutase, a key antioxidant enzyme that inhibits the production of oxygen free radicals. Zinc deficiency causes an increase in serum IgE levels and increased production of pro-inflammatory cytokines, thereby exacerbating the skin symptoms of atopic dermatitis [21]. Zinc also participates in the production of prostaglandins that regulate the secretory functions of the skin and affect collagen metabolism, which is why it is also responsible for skin regeneration. Zinc deficiency weakens the immune system, which makes it more prone to dermatitis and allergies.

The effect of zinc in people with vitiligo

Numerous studies suggest that there may also be a correlation between the concentration of zinc in the body and the severity of acquired vitiligo. Zinc deficiency causes a weakening of the immune system, which can trigger autoimmunity and the destruction of melanocytes, resulting in depigmentation. Zinc forms a zinc glycoprotein a2 (ZAG), which is responsible for the proliferation and regulation of melanocyte activity [23]. The absence of ZAG protein inhibits the proliferation of melanocytes and disrupts their maturation and differentiation process. Zinc ions are necessary for melanogenesis to proceed correctly. However, there is no evidence confirming the effectiveness of zinc supplementation in the treatment of acquired vitiligo, so further research is necessary.

Conclusions

Zinc is increasingly used in supplementation. Because it is not stored in the body, some people may experience a deficiency. Mild zinc deficiencies are common worldwide and can often be associated with dermatological diseases. Severe deficiencies are less common, coexist with deficiencies of other elements, and are most often associated with impaired intestinal absorption. The main factor causing zinc deficiency in developed countries is a vegetarian diet. Excess phytates in the diet limit zinc absorption. Zinc deficiency has a confirmed effect on weakening the immune system, impaired wound healing, and fertility disorders. It is also observed in people with atopic dermatitis and acquired vitiligo and is associated with impaired wound healing. It also affects thyroid function. Zinc is also used externally in cosmetology and dermatology. Zinc is being used more and more often due to its properties. Further research should be conducted to allow it to be used in the treatment of even more diseases.

Disclosures

Author's contribution:
Conceptualization – Monika Klimczak;
Methodology – Aleksandra Woskowska;
Software – Anna Hanslik;
Analysis – Magdalena Mendak;
Investigation – Agata Białek;
Resources - Magdalena Domisiewicz;
Data curation – Aleksandra Woskowska, Magdalena Domisiewicz;
Writing – Monika Klimczak;
Preparation - Anna Hanslik;
Visualization - Agata Białek, Anna Hanslik;
Supervision - Aleksandra Woskowska;
Project administration - Monika Klimczak, Magdalena Mendak; receiving funding not applicable.

All authors have read and agreed with the published version of the manuscript.

Funding Statement: This Research received no external funding.
Institutional Review Board Statement: Not applicable
Informed Consent Statement: Not applicable.
Data Availability Statement: The authors confirm that the data supporting the findings of this study are available within the article's bibliography
Conflicts of Interests: Authors declare no conflict of interests.

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