

## REVIEW ARTICLE

**Zinc as an Essential Nutritional Component of Human Body: A Systemic Review**Mehrangiz Ghaffari<sup>1</sup>, Mostafa Arabyaghoubi<sup>2\*</sup><sup>1</sup>Department of Pathology, Zabol University of Medical Sciences, Zabol, Iran, <sup>2</sup>Department of Anesthesiology, Zabol University of Medical Sciences, Zabol, Iran**Received: 15 April 2018; Revised: 28 May 2018; Accepted: 20 June 2018****ABSTRACT**

Second to iron, zinc, which is widely distributed in the human body, is the most abundant element in human body. The human body has about 2–3 g of zinc, with the highest concentrations in the liver, pancreas, kidneys, bones, and muscles. Other tissues with a higher concentration of zinc include parts of the eye, prostate gland, spermatozoa, skin, hair, fingernail, and toenails. Searches were conducted by two independent researchers in international (PubMed, Web of science, Scopus, and Google scholar) and national (SID and Magiran) databases for related studies from the inception of the databases to September 2017 (without time limitation) in English and Persian languages. To ensure literature saturation, the reference lists of included studies or relevant reviews identified through the search were scanned. Absorption and excretion of zinc are carried out through homeostatic mechanisms that are not quite well known yet. The absorption mechanism consists of two paths. Albumin is the most important zinc plasma carrier. The amount transported in blood, in addition to zinc, depends on the availability of albumin. Zinc is a single intracellular ion with structural, catalytic, and regulatory roles. Zinc plays important structural roles as part of a multiprotein structure.

**Keywords:** Component, Essential nutritional, Human body, Zinc**INTRODUCTION**

Second to iron, zinc, which is widely distributed in the human body, is the most abundant element in human body. The human body has about 2–3 g of zinc, with the highest concentrations in the liver, pancreas, kidneys, bones, and muscles. Other tissues with a higher concentration of zinc include parts of the eye, prostate gland, spermatozoa, skin, hair, fingernail, and toenails.<sup>[1]</sup> Zinc is a mainly intracellular ion associated with more than 300 different enzymes (in different enzyme groups and categories). Although zinc is abundant in cytosol, it is almost attached to proteins; however, the attached portion is in balance with a small ionic component.<sup>[2]</sup>

**MATERIALS AND METHODS****Search strategy**

Searches were conducted by two independent researchers in international (PubMed, Web of

science, Scopus, and Google scholar) and national (SID and Magiran) databases for related studies from the inception of the databases to September 2017 (without time limitation) in English and Persian languages. To ensure literature saturation, the reference lists of included studies or relevant reviews identified through the search were scanned. The specific search strategies were created by a Health Sciences Librarian with expertise in systematic review search using the MESH terms and free terms according to the PRESS standard. After the MEDLINE strategy was finalized, it was adapted to search in other databases. Accordingly, PROSPERO was searched for ongoing or recently related completed systematic reviews. The key words used in the search strategy were “zinc, essential nutritional, component, and human body” which were combined with Boolean operators including AND, OR, and NOT.

**Study selection**

Results of the literature review were exported to endnote. Before the formal screening process, a calibration exercise was undertaken to pilot and refine the screening. Formal screening process

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of titles and abstracts was conducted by two researchers according to the eligibility criteria, and consensus method was used for solving controversies among the two researchers. The full text was obtained for all titles that met the inclusion criteria. Additional information was retrieved from the study authors to resolve queries regarding the eligibility criteria. The reasons for the exclusion criteria were recorded. Neither of the review authors was blinded to the journal titles, the study authors, or institutions.

### Absorption, transfer, storage, disposal

Absorption and excretion of zinc are carried out through hemostatic mechanisms that are not quite well known yet. The absorption mechanism consists of two paths. The saturated carrier mechanism operates in low-level receptacles (low luminosity concentration), and the inactive mechanism also operates at high loading times and high lumens concentration. The solubility of zinc in the digestive lumen is vital.<sup>[3]</sup> Zinc ions are mainly attached to small amino acids or peptides in the lumen of the intestine and are released on the tight junctions and are absorbed by the carrier mechanism (hZIP family). The entry into the tight junction's stem cells is associated with the binding of zinc ions to metallothionein and other cytosolic proteins of absorption cells.<sup>[4]</sup> Metallothionein transfers zinc to the lateral part of the body, and zinc is removed from the cell and transported to the bloodstream. Since the concentration of zinc in the blood is much higher than cytosol of the absorption cells, the removal stage is carried out through the active transfer mechanism [Figure 1].<sup>[5]</sup> The absorption of zinc is affected by the amount of food and the presence of other interventional agents (especially phytates) in the diet. After consuming food, the concentration is increased then decreases through a dose-response pattern process. High-protein foods result in increased zinc absorption through the formation of Zn-amino acids (which make zinc more absorbable).<sup>[6]</sup> The absorption of zinc increases slightly during pregnancy and lactation. Zinc is absorbed first through the portal vein to the liver; then, it is distributed among different tissues. Absorption disorders are closely associated with several intestinal disorders such as Crohn's disease or inappropriate pancreatitis.<sup>[7]</sup>

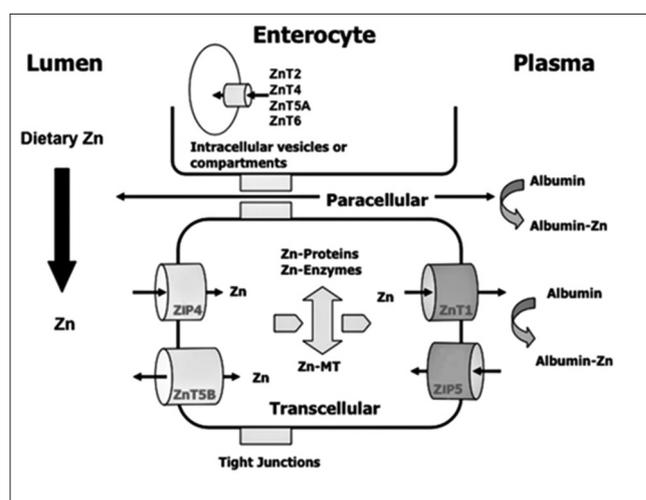


Figure 1: Zinc absorption and transfer

### Transmission in the blood

Albumin is the most important zinc plasma carrier. The amount transported in blood, in addition to zinc, depends on the availability of albumin. A small portion of zinc is also transported by transferrin and alpha-2 macroglobulins.<sup>[8]</sup> The major part of the zinc is in the blood, inside the erythrocytes and leukocytes. Plasma is metabolically active and its levels change in response to dietary intake and physiological factors such as injury and inflammation. Zinc levels decrease down to 50% in response to the acute phase of the injury, which is a possible cause of retention in the liver.<sup>[9]</sup>

### Intestinal excretion

Zinc is excreted through feces in healthy individuals. When zinc is received intravenously, about 10% of the dose is received in the liver after 30 min. However, in cases of hunger, nephrosis, diabetes, alcoholism, liver cirrhosis, and porphyry, the excretion of zinc increases through urine. Plasma and urinary concentrations of histidine and cysteine zinc and other metabolites may be associated with increased zinc loss in these patients.<sup>[10]</sup>

### Function

Zinc is a single intracellular ion with structural, catalytic, and regulatory roles. Zinc plays important structural roles as part of a multiprotein structure. It is also associated with 300 different enzymes and is involved in the synthesis or decomposition of carbohydrates, fats, proteins, and nucleic acids.

It also functions as an intracellular signal in the brain cells and is stored in synaptic vesicles; it is essential for the normal functioning of the central nervous system. In addition, zinc stabilizes the structure of proteins and nucleic acids, as well as the integrity of subcellular organelles and transport processes.<sup>[11]</sup>

### **Metallothionein**

Metallothionein is the most abundant non-enzymatic protein containing zinc. This low molecular weight protein is rich in cysteine and contains exceptionally large amounts of metal that has zinc; it, also, carries less amounts of copper, iron, cadmium, and mercury. The biological role of metallothionein is not clearly known, but it plays a functional role in the absorption of zinc. Metallothionein, as an intracellular reservoir, may act as a protease inhibitor or a controlling agent and it may decrease the oxidative stress (especially in high-stressed cells).<sup>[12]</sup> Hence, metallothionein may play a role in detoxifying metals as well as absorbing them.

High dosage of zinc in the nucleus leads to the stabilization of the DNA and RNA structure and is essential for the activity of RNA polymerase in cell division. Zinc is present in the chromatin proteins involved in transcription and replication and is protective against degenerative-macular degenerative disease. Although zinc and nasal spray gluconate tablets are widely used to treat or prevent common colds, they do not seem to be quite effective.<sup>[13]</sup>

### **Using diet reference**

The intake of zinc dietary reference intake (DRI) is 11 mg/day in male and female adolescents. Due to the lower weight of adolescent and adult women, their DRI is 8–9 mg/day. The essential rate is 8 mg per before adolescence. Infants' DRI is 2 mg/day for the first 6 months of life and 3 mg/day for the second 6 months.<sup>[14]</sup>

### **Nutrition resources and intake**

In most Americans, the vast majority of zinc recipes come from consuming meat, fish, poultry, ready-to-eat zinc-enriched breakfast cereals, milk, and its products. The shellfish contain a high

amount of zinc; other Mollusca, grains, dry beans, and nuts are good sources of zinc. In general, zinc intake is associated with protein intake.

The content on the normal diet of adults in our western countries varies from 10 to 15 g/day. Women need to receive less energy due to lower energy consumption. The density of zinc within the diet of an adult American is about 5.6 g per 1000 kilocalories.<sup>[15]</sup>

### **Zinc deficiency**

The clinical signs of zinc deficiency include shortness of height, hypogonadism, mild anemia, and low plasma zinc levels. Zinc deficiency leads to multiple immunological disorders. Severe zinc deficiency leads to thrombosis, lymphopenia, proliferative response of lymphocytes to mitochondria, selective reduction of T-helper cells, decreased activity of NK cells, insomnia, and decreased thymus hormone activity; however, mild zinc deficiency can lead to reduced immune functions, such as interleukin-2 production impairment.<sup>[16]</sup> Zinc supplements may improve immune function, but more evidence is required to do further studies. Mild zinc deficiency has been reported to be associated with boredom, fatigue, and decreased activity of NK cells; however, this form of deficiency is not related to thromboses and lymphopenia atrophy. The similarities between patients with sickle cell anemia and zinc deficiency indicate the possibility of a secondary zinc deficiency in anemia patients.<sup>[17]</sup>

### **Poisoning**

Poisoning due to oral intake of zinc (100–300 mg/day) is rare; however, in case of necessity, the maximum amount is 40 mg/day for adults. Excessive supplementation of zinc interferes with the absorption of copper. The major problem of zinc poisoning occurs in patients with renal failure who are undergoing dialysis due to the contamination of dialysis fluids or sticky plastics used in spiral dialysis or in galvanized tubes. The syndrome of poisoning in these patients is characterized by anemia, fever, and dysfunction of the central nervous system. Taking more than 2 g or more zinc sulfate per day may cause gastric disorders and vomiting. Inhalation of zinc vapors during welding is toxic, but it can be prevented by taking precautionary measures.<sup>[18]</sup>

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