

Zinc: A Mineral of Complex Biological Activity

The essentiality of zinc for the growth of micro-organisms, plants, and animals has been known for six decades. However, until 1961 it was believed that zinc deficiency in humans could never occur.

It is known today that zinc deficiency is widely prevalent and the morbidities associated with zinc deficiency are severe (Prasad A, BMJ 2003; 326:409-410). Zinc, an essential trace mineral, possesses a complex biology, being omnipresent and versatile. It is required in gene expression and the regulation of cellular growth and differentiation, resulting from its participation as a co-factor in more than 120 enzymes implicated in the metabolism of nucleic acids, carbohydrates and proteins. This makes it a key to DNA, RNA, and protein synthesis as well as playing important roles in immune system function and male reproductive function. Its deficiency leads to the deterioration of many metabolic functions, and it is vital during life periods of growth and cell differentiation, such as pregnancy and childhood (Camara and Amaro, Int J Food Sciences and Nutr 54;143-151:2003).

Deficiencies of zinc have been linked to:

- Delayed skeletal maturation and defective mineralization of bone
- Weight loss
- Intercurrent infections
- Hypogonadism (Males)
- Lack of sexual development (Females)
- Growth retardation
- Dwarfism
- Delayed puberty in adolescents
- Rough skin
- Poor appetite
- Mental lethargy
- Delayed wound healing
- Short stature
- Diarrhea
- Pneumonia
- Stretch marks (striae)
- White spots on finger nails
- Reduction in collagen
- Acne
- Poor immune system
- Cross-linking of collagen
- Hyaluronic acid abnormalities
- Defective connective tissue
- Macular degeneration
- Cataracts
- Insulin resistance

Zinc Availability

The absorption of zinc at the intestinal level takes place via a saturable active transport system as well as a non-saturable passive diffusion process. High levels of zinc in the lumen will limit the amount of zinc absorbed via the active transport system due to limited receptors. The passive diffusion process depends on the concentration gradient of the zinc cation for absorption. There are multiple factors that can have an impact on zinc absorption (see Figure 1).

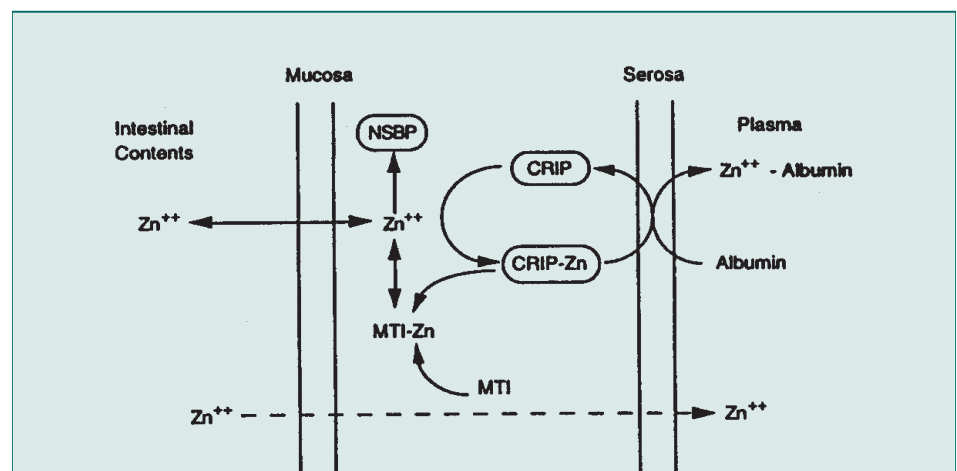


Fig 1. Intestinal Zinc Absorption. Passive diffusion is shown at the lower part of the diagram while active transport involving metallothionein 1 (MTI), the cysteine-rich protein (CRIP), and the nonspecific binding proteins (NSBP) is shown in the upper portion of the diagram.

Compounds that are known to enhance zinc absorption include amino acids such as glycine, histidine, lysine, cysteine, and methionine, picolinic acid (secreted by the pancreas), vitamin B6 (it increases picolinic acid secretion), and citrate (Camara and Amaro, *Int J of Food Sci and Nutr*; 54, 143-151:2003). Additionally, animal protein can improve zinc absorption. Studies have shown that animal protein affects zinc availability in two ways. It increases the presence of zinc in the diet thus increasing the zinc cation gradient for passive diffusion, and the intermediate products produced in protein digestion bind to zinc and facilitate its absorption (Lonnerdal B, *J Nutr* 130, 1378s:2000) (Sandstrom B, *Proc Nutr Soc* 51, 211-210:1992). Some research has indicated that the higher the sulfhydryl level in a protein, the greater the increase in mineral bioavailability.

Compounds that have been shown to inhibit the absorption of zinc are selenium, calcium, iron, folic acid, phytic acid, tannins, and fiber. The actual body content of zinc has a major influence on the availability of

NOTE:

The typical US diet provides between 4 and 14 mg of zinc per day. The established US RDA for zinc is 15 mg for adult males, and 12 mg for adult females. Zinc is relatively poorly absorbed, with an average absorption rate from 10-40%. The higher the grain and vegetable content of the diet (particularly high fiber grain product), the lower zinc's overall relative bioavailability. US women have a reported mean intake of zinc that is only 70% of the RDA.

zinc. The higher the zinc content of the individual, the lower the relative zinc absorption will be. Previous studies (Ziegler EE, et al, *J Nutr*, 119, 1661-1669:1989) have shown that children who received pre-trial courses of zinc supplementation had a lower relative absorption of zinc than a similar group of children who had not received pre-trial zinc supplementation. August, et al. (*Am J Clin Nutr* 50, 1457-1463:1989) found that in young adults the zinc percentage of absorption was 64% when the zinc content of the diet was 2.8-5 mg/day, and that it decreases to 39% when it contained 12.8-15 mg/day.

Various zinc-mineral interactions have been investigated. It has been shown (Gunshin H, et al., *Nature* 388, 482-488:1997) that there is a divalent cation transporter with broad specificity in the brush border membrane. This transporter is a multivalent metal channel, and it could explain numerous interactions between zinc and the other divalent cations due to competition for this common transporter. The metal cations of calcium, magnesium, iron, copper, and manganese have all been shown to be capable of inhibiting zinc by competing for transport across the brush border membrane. Some feel that multiple transporters may be involved in the various metal-metal interactions observed.

More recently, fructo-oligosaccharides have been shown to decrease the ability of phytic acids to inhibit zinc's absorption, possibly by forming water soluble compounds with zinc and preventing the formation

of the insoluble (non-absorbable) zinc phytate compounds. Researchers have proposed that some saccharides, such as lactose and glucose polymers could improve zinc absorption at the brush border membrane. However further investigations need to be done on that theory.

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Absorption Pathways

The factors that are of concern in zinc availability all hinge on the fact that zinc is ionized in the gut prior to absorption. The factors that decrease or enhance zinc absorption do so to the ionized (cationic) form of zinc. The zinc manufactured by Albion is a totally reacted, nutritionally functional zinc amino acid chelate. As such, it is not handled in the gut in the same way as the typical zinc salt forms. It has been stated that this form of zinc is absorbed as an intact chelate - not ionized. The study on the metabolism of Albion's Zinc Chelazome® (Zinc bisglycinate chelate) abstracted below was reported at the annual FASEB meeting in 1995.

Metabolism of Zinc-Bisglycinate Chelate: A Preliminary Study.
SD Ashmead, M. Funk-Archuleta, E. Ellis, RD Lloyd, HD Ashmead.
University of Utah and Albion Laboratories.

Twenty-four male Sprague-Dawley rats were used to examine the metabolism of zinc-glycine chelate in the form of zinc-bisglycinate. The animals were randomly divided into three groups of equal size: zinc only, glycine only, and the chelate. All rats were maintained on a zinc deficient

semipurified diet for a period of 2 weeks. After fasting overnight, the rats in the zinc only group received 5 mg of ZnCl₂ containing 6.5 microCuries of ⁶⁵Zn; the rats in the glycine only group received 11 mg of glycine containing 54.5 microCuries of ³H-glycine; the rats in the chelate group received both radio labels in the same amounts in the form of the zinc-glycine chelate. Two hours following treatment, the animals were sacrificed under anesthesia via angular exsanguinations. Red blood cells, serum, bone, liver, kidney, brain, and testes samples were removed and analyzed for their respective radio labels depending on the treatment received. Although at the time of sampling the tissue levels of ⁶⁵Zn in the tissues tested were similar for the zinc chloride and the zinc-glycine chelate group, there was far less variability to the tissue levels for the zinc-glycine chelate group. In fact the standard of deviation (variability) for the chelate groups was about half that of the zinc chloride group. This

would indicate that the absorption of the chelate form is less impacted by the genetics or intestinal environment of the animal. This gives evidence to the absorption of the chelate being better controlled and suggests that the chelate absorption is via different pathway. Additionally, the ³H-glycine levels were different for the glycine-only versus the zinc-glycine chelate group. The levels of the ³H-glycine were about the same at the liver tissue, but were lower at the subsequent tissues. The fact that the ³H-glycine levels are lower at the subsequent tissues tested would indicate that the zinc chelate is metabolized at the target tissue, and the amount of glycine found in the tissue is limited by the zinc requirement of the target tissue. The researchers concluded that the zinc-glycine chelate is absorbed intact, and metabolized differently than the zinc chloride.

Zinc-Mineral Interactions

NOTE:

Zinc status can be difficult to assess accurately. Frank deficiency can be readily diagnosed in the laboratory, but marginal deficiency is extremely difficult to confirm. Plasma and neutrophil levels can give a static measure of zinc status, but tell only the level of zinc in transport, not the functional state of the individual. Measurement of certain zinc-requiring enzyme levels, such as carbonic anhydrase and 5' nucleotidase are better indicators, since they are sensitive to shorter term zinc deprivation.

Other nutritionally important minerals such as calcium or iron (divalent metals in particular) are stated to hinder the absorption of zinc, probably by competing for the divalent metal transporter that aids in the absorption of the cationic form of these metals. Albion's Zinc Chelazome® should not require this divalent metal transporter, since it does not ionize in the gut the way the typical zinc salts do. This characteristic of Albion's zinc chelate should decrease the potential for other divalent metals to hinder absorption of this zinc form. The animal study summarized below supports this point.

Zinc source influences zinc retention in hair and hair growth in the dog.

J Lowe, J Wiseman, and DJA Cole.

J Nutr 124:2575S-2576S, 1994.

In this study the researchers added zinc from three different sources to a typical commercial dog diet formulation that contained no added zinc. The zinc sources were zinc

Figure 2.

Effect of Zinc Source and Calcium Content of the Diet of Zinc Absorption, Retention and Hair Growth			
Treatments	Faecal Zinc	Hair Growth Rate	Zinc Deposited in Hair
	Mg · kg ⁻¹ · d ⁻¹	Mg · d ⁻¹ · 10 cm ⁻²	Mg · 25 d ⁻¹ · 10 cm ⁻²
ZO	3.03b	4.775b	10.83b
ZO+c	4.02a	3.000d	7.28c
ZM	2.75d	6.025a	21.09a
ZM+C	2.74d	6.063a	21.15a
ZP	2.59a	5.215b	11.73b
ZP+C	2.90c	4.183c	9.91b
SED	0.02	0.244	0.90

SED, standard error of the difference. Means in the same column with different superscripts differ significantly at P<0.05. ZO, 50 mg Zn · Kg⁻¹ from zinc-polysaccharide complex; +C denotes the addition of 20 grams Ca · Kg⁻¹; 4 dogs pretreatment.

oxide, zinc polysaccharide complex, and zinc amino acid chelate (Albion). The dogs were given 50 mg/kg of elemental zinc for 2 weeks (after they all received an acclimatization diet that had 50 mg/kg of zinc from zinc oxide for the previous 2 weeks). The researchers then duplicated this treatment, but with the addition of 20 grams/kg of additional calcium over 2 weeks. The results are listed in Figure 1. The amount of fecal zinc was significantly greater in the presence of calcium, except when the zinc source was the zinc amino acid chelate (Albion). Zinc excretion (an indicator of the unabsorbed zinc) was far greater for the zinc oxide group. Hair growth and the amount of zinc deposited in hair was far greater for the zinc amino acid chelate (Albion) group. The researchers concluded that the calcium did not negatively impact the zinc from Albion's zinc amino acid chelate, and that the greater hair growth and zinc hair content seen in the dogs fed the Albion zinc amino acid chelate was a clear indication that this was the form that had superior bioavailability.

Conclusion

As research mounts, the importance of zinc to human health becomes more and more evident. Deficiencies in zinc intake and availability result in potentially devastating crises in the biological function of the immune system, in glucose metabolism, growth, hormonal balance, and wound healing. There is a worldwide problem surrounding the adequate intake of this vital trace mineral. The availability of zinc is affected by more than just the presence of this mineral in one's diet. The bioavailability of this mineral is impacted by so many variables. Diets that are more reliant on vegetables and grains as food sources tend to lead to even greater risks for zinc deficiencies. It is important that the fortification and/or the supplementation of zinc be done with intelligent selection of zinc that is most bioavailable.

Albion's totally reacted zinc amino acid chelates (Zinc Chelazome®, Zinc Arginine Amino Acid Chelate, and Zinc Histidine Amino Acid Chelate) are

a form of zinc that is best absorbed in the face of all the factors that are known to negatively impact zinc absorption. Fortification of grains is a common way to deliver zinc in the food supply. The phytates found in the fibers of various grains do not decrease the absorption of Albion's zinc amino acid chelate, the way it does with other zinc forms. Dietary supplements that use this form of zinc have less dietary absorption interference and better relative absorption than other forms of zinc.

More studies will soon be published that point to the better absorption and safety of this patented form of zinc.

CAUTION:

Zinc associated with metallothionein in the liver has a half life of 2 weeks, and it is readily mobilized. The body will use this as a source of zinc during periods of zinc dietary deprivation. However, the size of this pool of zinc is very small (less than 170 mg), and thus zinc depletion can become functionally relevant within a week!

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