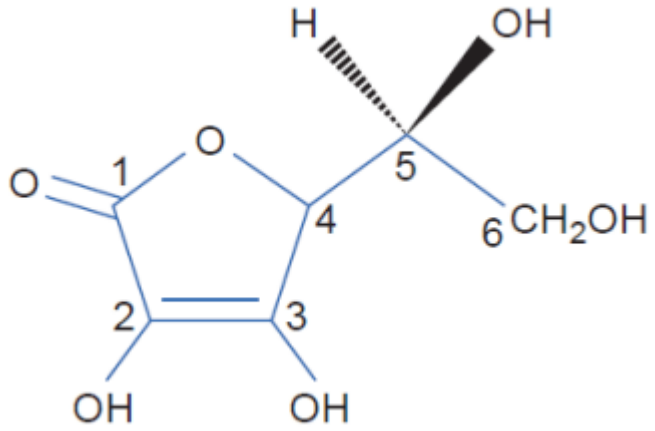
Zinc, Vitamin C Synergy and Immune Function

The world is facing an unprecedented health crisis due to the Covid-19 pandemic. The virus has been spreading steadily around the world since its first outbreak in December 2019 in Wuhan. It has resulted in more than 300 million cases of infection worldwide and over 5 million deaths. Due to its global spread and high death toll, this disease and its consequences represent a very current challenge for research and development of new therapeutic approaches, one of which is vitamin C and zinc therapy. Recent studies have found that intravenous infusion of vitamin C significantly reduced mortality and days in the intensive care unit and reduced inflammation in covid-19 patients and studies suggest that vitamin C administration may increase survival by attenuating the excessive activation of immune responses – the 'cytokine storm'. Zinc thus has potential health benefits against pandemic COVID-19 by improving the immune response, minimizing infection and inflammation, preventing lung damage, and inhibiting viral replication. It would therefore be unjustified to claim that vitamin c and zinc are the miracle answer to the coronavirus pandemic, but it would be fair to say that there is new evidence in favor of their supplementation in COVID-19.

Vitamin C

Vitamin C is known as L-ascorbic acid because it has been observed to be the necessary factor in the treatment of scurvy (*Latin scorbutus, hence 'a-scorbutus'*).
In general, the term also includes its oxidised form, L-dehydroascorbic acid, which can easily be converted to L-ascorbic acid in the human body. It consists of an unsaturated lactone ring, substituted with two primary alcohol functions

and a ketone group.



Structure of vitamin C

Food sources

Vitamin C is found in large quantities in citrus fruits, red berries (blackcurrant, strawberry, redcurrant and raspberry), kiwi fruit and cabbage.

Pharmaceutical forms

VIT C 1000 SUGAR-FREE, effervescent tablets 1g box of 10.

Hypo and hypervitaminosis C

Vitamin C deficiency

Vitamin C deficiency is responsible for scurvy in adults and Barlow’s disease in children.

Scurvy in adults

In its ultimate form, scurvy is characterised by joint manifestations, subcutaneous and intramuscular haemorrhages, oedema of the lower limbs, neuropathy and cerebral haemorrhage, which can be fatal if left untreated.

Vitamin C deficiency leads to changes in the structure of collagen, resulting in a haemorrhagic syndrome with petechial

purpura centred on the hair follicles, ecchymosis and haematomas, haemarthrosis, sub-periosteal hemorrhages responsible for bone pain (arthralgia of the knees, ankles and shoulders), haemorrhages in the nerve sheaths causing “the painful paralysis of scurvy”.

At an advanced stage and in the absence of treatment, people with scurvy die from severe hemorrhages, superinfection, and arterial hypotension. A scorbutic state has to be suspected, even in industrialized countries, in the presence of skin lesions (hyperkeratosis, erythema, purpura, perifollicular hemorrhages), gingival bleeding, particularly in chronic alcoholics, elderly people living in institutions In addition, there are several pathologies and other situations in which the level of vitamin C drops in plasma such as surgery, trauma, sepsis, burns and in very serious injuries, also observed in cancer patients. Acute myocardial infarction is also associated with rapid loss of vitamin C in both plasma and tissue.

Infantile scurvy (Barlow’s disease) In children, the first clinical symptoms are usually severe bone pain in the lower limbs secondary to subperiosteal hemorrhage, resulting in lameness and even inability to walk. Associated with an alteration of the general state (loss of appetite, weight loss, irritability) it may mimic a hematological or tumoral pathology. Cases are rare before the age of 6 months, because vitamin C is present in breast milk (in the absence of maternal deficiency) and in artificial infant milks.

Hypervitaminosis

There is no known vitamin C intoxication, the excess being eliminated in the urine and feces in both original and metabolized form.

Furthermore, vitamin C is very well tolerated, with very few side effects reported:

A slight excitatory effect preventing sleep diarrhea abdominal bloating appearance of kidney stones may occur for large ingested doses.

Contraindications to the use of vitamin C are exceptional:

hyperoxaluria (urinary oxalate excretion increases at doses greater than 1 g per day, which favors the formation of calcium oxalate stones), G6PD deficiency (high amounts of vitamin C can trigger hemolysis), and situations that are aggravated by an acid load (gout, cirrhosis, renal tubular acidosis, paroxysmal nocturnal hemoglobinuria).

Biochemical functions and physiological roles of Vitamin C

Biochemical functions and physiological roles include:

Hydroxylation reactions, Collagen synthesis, Catecholamine synthesis, Carnitine synthesis, Iron metabolism, Immune response, and Antioxidant action.

Vitamin C and the Immune system

Vitamin C has a potential role in improving the function of innate immunity and enhancing cellular and humoral immune responses. Evidence has shown that inadequate micronutrient intake, including vitamin C, decreases resistance to infection and increases disease complications.

Vitamin C supplementation in mice increased the release of interferon, which plays an important role in enhancing the cellular immune response against viral infection. In addition, the administration of high-dose oral vitamin C (60 mg/kg) enhanced the activity of natural killer cells, which play an important role in innate immunity against viral infections. Apparently, vitamin C accumulates intracellularly in neutrophils, which may suggest that vitamin C plays a role in

maintaining normal leukocyte function. Interestingly, several studies have shown that the effect of vitamin C on neutrophil phagocytic function is dose-dependent. Vitamin C supplementation at a dose of 200 mg to 1 g per day for 1 to 4 months improved neutrophil phagocytic activity.

Other evidence has shown that vitamin C improves T-cell proliferation, differentiation, and maturation in vitro.

In fact, SARS-CoV-2 infection has a significant negative impact on the immune system. This leads to lymphopenia and a reduction in the number of natural killer cells in addition to inducing an excessive release of inflammatory mediators leading to a cytokine storm and tissue damage. Based on the above findings, vitamin C may have the potential to ameliorate the deleterious immunological effect of SARS-CoV-2 infection, which may make it a feasible treatment option in COVID-19.

Zinc

Zinc is an essential oligo-element, it is present in very small quantities in the body, about 2 g, of which nearly 70% is found in the bones, skin and hair, with a normal plasma concentration of 11 to 20 µmol/L which is maintained by dietary intake.

Food sources

The foods that are richest in zinc include fish, seafood, red meats, whole grains, and pulses.

Pharmaceutical forms

Zinc 45mg, effervescent tablets, box of 20.

Zinc deficiency

The main risk factors for zinc deficiency include: a diet low

in zinc or high in phytates, disorders related to malabsorption (which may be due to diarrhea or intestinal parasites), liver cirrhosis and repeated dialysis, and certain genetic diseases. Advanced age.

Among the pathological conditions that appear to be the consequence of nutritional zinc deficiency in humans include: Growth retardation and delayed puberty in children. Fetal malformation or hypotrophy in pregnant women. Prostatic hyperplasia in men, affecting reproductive function and fertility.

Gastrointestinal signs: digestive disorders, diarrhea anorexia and changes in taste and smell (dysgeusia and dysosmia)

Skin signs: poor skin healing, alopecia, rash or eczema. Ophthalmic signs: blepharitis, conjunctivitis, photophobia, and corneal opacities.

Also increased risk of infectious diseases, and lymphocyte immune disorders mediated by T cells are corrected by zinc by zinc supplementation.

Hyperzincemia

Zinc intoxication is very unusual because there is a wide gap between the amount of zinc needed to meet nutritional requirements and the toxic dose. However, prolonged exposure to amounts in excess of the tolerable upper intake level can cause adverse effects including Metallic taste, nausea, vomiting, diarrhea, abdominal cramps, decreased immunity, decreased high-density lipoprotein cholesterol levels, as well as microcytic hypochromic anemia and copper deficiency which can lead to neurological problems.

Biochemical functions and physiological

roles

Zinc is an essential micronutrient involved in numerous catalytic, structural, and regulatory functions.

Nearly 300 different enzymes depend on zinc for their ability to catalyze vital chemical reactions, and it is involved in various steps of protein synthesis, including activation of enzymes involved in nucleic acid synthesis, histone regulation, DNA repair, and initiation of genome reading via transcription factors (“zinc finger” proteins).

Zinc is also involved in the activity of certain hormones such as insulin, prostaglandins, testosterone, prolactin, thymulin and growth hormone. It is also involved in the maintenance of taste and smell functions. Finally, zinc is a cofactor of superoxide dismutase (Cu, Zn, SOD), which plays a particularly important role in the detoxification of free radicals, and carbonic anhydrase, which is necessary for the maintenance of acid-base balance. → All these roles imply that our trace element plays various physiological functions:

Zinc and Men’s Health

Zinc is essential for maintaining normal serum testosterone. Insufficient zinc levels prevent the pituitary gland from releasing luteinizing and follicle-stimulating hormones, which stimulate testosterone production. Zinc also inhibits the enzyme aromatase, which converts testosterone into excess estrogen. In addition to the impact on hormone levels, zinc has also been shown to help the body produce healthier sperm by increasing sperm count and motility. Research published in the American Journal of Clinical Nutrition found that male volunteers who consumed low amounts of zinc had decreased semen volumes and serum testosterone concentrations.

Zinc and Skin

Zinc is essential for healthy skin. Topical preparations of

zinc (zinc oxide) have been used as an astringent to treat diaper rash itching and chapped lips. Zinc sulfate in a water-based solution has been used to treat acne, cold sores, and burns. Internally, zinc stimulates cell division, healing, and proper formation of connective tissue formation, and increases the transport of vitamin A from the liver to the skin to the skin, helping to protect body tissues from damage and to repair damage present.

Zinc during pregnancy and lactation

Because of zinc's role in cell generation, it is essential for the developing fetus where cells divide rapidly, so an adequate amount of zinc in the pregnant woman's diet also reduces the risk of premature birth and other complications and has been shown to improve neonatal survival. Research has shown that by the sixth month of lactation, even a well-nourished mother can provide less zinc than a Research has shown that by the sixth month of lactation, even a well-nourished mother may be providing less zinc than is needed for her child. The breastfed babies who received zinc supplements increased significantly in height and weight compared to those who received a placebo.

Zinc and the immune system

Zinc plays a role in cell division and DNA replication, contributing to the production of immune system cells.

Zinc deficiency leads to immune dysfunction in innate immunity. Specifically, zinc deficiency reduces Natural Killer (NK) cell lytic activity, impairs NKT cell cytotoxicity, and immune signaling also increases the production of proinflammatory cytokines, such as interleukins IL-1β, IL-6, and tumor necrosis factor (TNF)-α. Since zinc is an essential cofactor for thymulin, a peptide hormone that plays a key role in T-cell maturation in the thymus, the acquired immune system is also impacted by zinc deficiency, it causes thymic atrophy and T-cell lymphopenia as well as a reduction in premature and

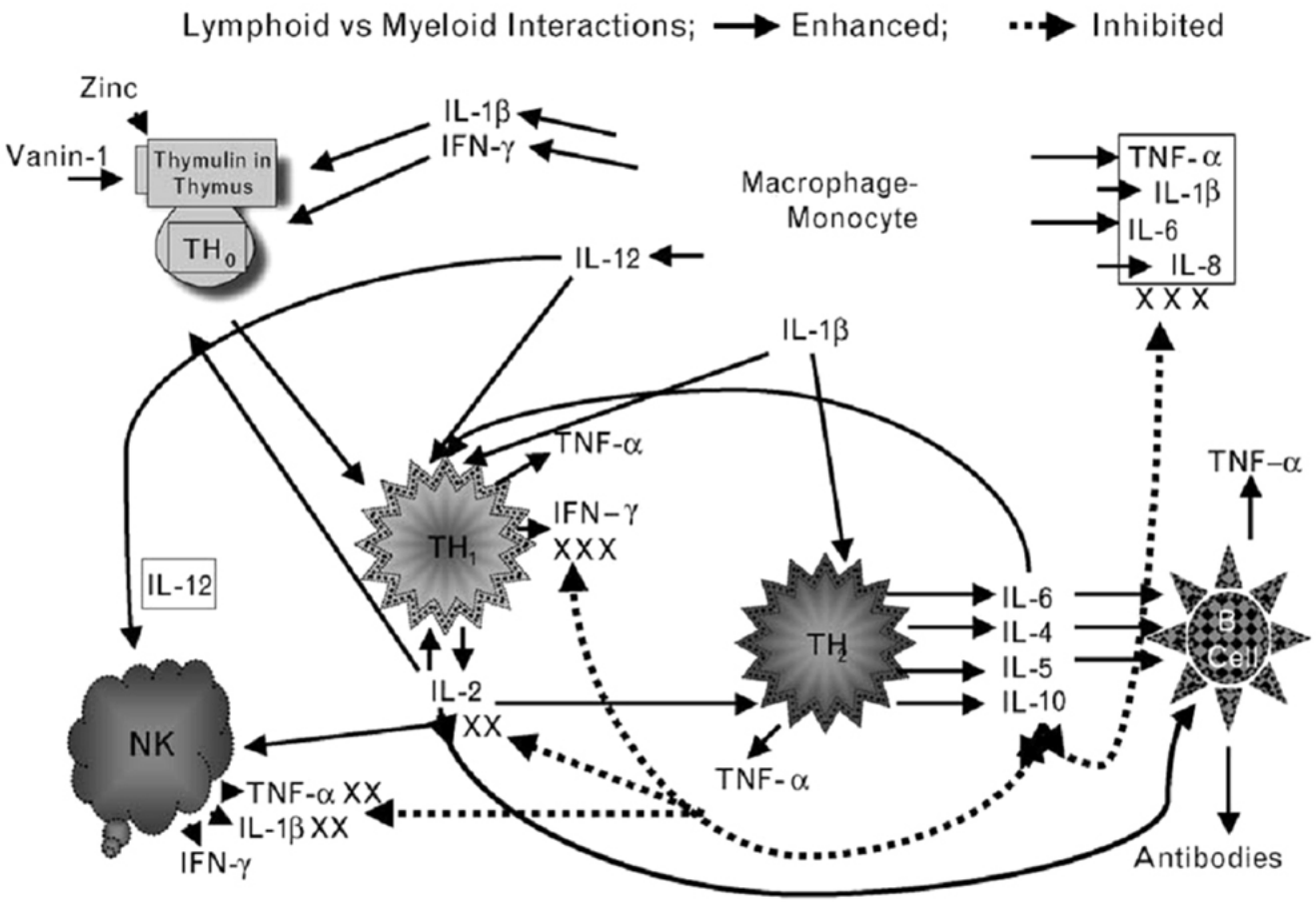
immature B-cells, and therefore antibody production is also reduced.

Zinc and the immune response

Zn treatment has been shown to increase the production of interferon α (IFNα) (proteins with antiviral, antiproliferative, and immunomodulatory properties) by leukocytes and potentiate its antiviral activity via JAK/STAT1 signaling, as observed for rhinovirus-infected cells.

One of the characteristics of COVID-19 is an unbalanced immune response. Due to hyper inflammation, immune products including proinflammatory cytokines such as interleukin (IL)-6, C-reactive protein (CRP), tumor necrosis factor (TNF)α, and IL-1β (summarized as cytokine storm), reactive oxygen and nitrogen species, tissue destruction, permanent lung damage, and death due to systemic inflammation and organ failure are expected, whereas the anti-inflammatory response is insufficient.

However, the anti-inflammatory activity of zinc has been demonstrated through regulation of T-cell function, inhibition of IκB kinase (IKK) activity, and subsequent nuclear factor kappa B (NF-κB) signaling with a concomitant reduction in proinflammatory cytokine production.



The anti-inflammatory property of zinc

The anti-inflammatory property of zinc is demonstrated by the inhibition of NF-κB translocation from the cytoplasm to the nucleus where it binds to pro-inflammatory genes leading to exaggerated production of proinflammatory cytokines and inflammatory mediators such as interleukin 1 beta (IL-1β), Interleukin 6 (IL-6), tumor necrosis factor-alpha (TNFα), integrins, intercellular adhesion molecule 1 (ICAM-1), vascular cell adhesion protein 1 (VCAM-1), inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX2) with disseminated intravascular coagulation and atherosclerosis.

As well as improving Zn status may also reduce the risk of bacterial coinfection by exerting a toxic effect on Streptococcus pneumoniae, reducing its growth by interfering with Mn (II) homeostasis and developing cytoplasmic manganese deficiency.

- Zinc improves cilia morphology and increases the frequency of ciliary beats, thereby improving

mucociliary clearance and rejection of particles containing bacteria and viruses.

- Zn can decrease the activity of ACE2, known to be the receptor for SARS-CoV-2, so it can block viral RNA replication through inhibition of RdRp
- Zinc regulation of antiviral immunity may also limit SARS-CoV-2 infection through upregulation of IFNα
- The anti-inflammatory activity of zinc, through regulation of T cell function and also through inhibition of IKK activity and NF-κB signaling, induces down-regulation of pro-inflammatory cytokine production.
- Modulation of bacterial Mn(II) homeostasis by zinc may inhibit the growth of S. pneumoniae and consequently reduce the risk of bacterial co-infection in viral pneumonia.

Vitamin C – Zn Synergy and the Immune system

According to (S. Beveridge et al., 2008) in their article Immune-enhancing role of vitamin C and zinc and effect on clinical conditions Vitamin C levels in plasma and white blood cells rapidly decrease during infections and stress. Vitamin C supplementation enhances components of the human immune system such as anti-microbial and natural killer (NK) cell activities, lymphocyte proliferation, chemotaxis and delayed hypersensitivity. Vitamin C contributes to the maintenance of the redox integrity of cells and thereby protects them from reactive oxygen species generated during the respiratory burst and inflammatory response.

Similarly, zinc deficiency affects cellular mediators of innate immunity such as phagocytosis, NK cell activity and generation of the oxidative burst.

Hence, both nutrients play significant and complementary roles in immune function and modulation of body resistance to

infectious agents, thereby reducing the risk, severity and duration of infectious diseases. and duration of infectious diseases. Deficiency of either of these essential nutrients impairs immunity, with vitamin C being crucial for cellular immunity A large number of randomized controlled intervention trials with intakes of 1 g of vitamin C and 30 mg of Zn have been conducted. These trials suggest that adequate intakes of vitamin C and Zn help improve symptoms and shorten the duration of respiratory tract infections, including common infections. symptoms and shorten the duration of respiratory tract infections, including the common cold. Natural defenses can only provide complete protection if the body has enough Zn.

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