



## Short Commentary

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# The Innovations Regarding the Use of Zinc and Selenium Ions in Cancer Therapy

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### Abstract

Zinc is part of the micronutrients class and it is essential for all organisms. The growth and development organisms in human subjects depend strictly on zinc. It is considered to be an indispensable mineral as it is necessary for the production of many enzymes vital to human organism, being a component of structural and regulatory proteins, including transcription factors, and forming so-called 'zinc fingers' (sequences which allow the transcription factors to be linked to DNA). Many studies have shown the link between the serum concentration of Zn<sup>2+</sup> ions and the concentration of certain cytokines. To date, several reviews have suggested antitumoral activities of zinc and its potential as a therapeutic strategy for cancer. Selenium is a strong antioxidant that has raised awareness within the researchers due to its anticancerous action. It is an essential component of several major metabolic pathways, the metabolism of thyroid hormones, the antioxidant defense systems and the immune function. The antioxidant activity is similar to that of vitamin E. The predominant biochemical action of selenium is to be antioxidant by the selenium-dependent enzyme, glutathione peroxidase and thus to protect the cell membranes. Many studies emphasize that both zinc and selenium are involved in cancer prevention, particularly through the disturbance of the cancer mechanism and the inhibition of malignant cells.

**Keywords:** Selenium; Zinc; Cancer; Antioxidant.

### Material and methods

We retrieved studies from the PubMed database and systematically reviewed both the mechanisms and biological activity of zinc and selenium with regard to oncological disorders. Interactions between these two and other chemical compounds were also discussed.

### Results

In vitro, studies have discovered that selenium exhibits growth-inhibition effects on malignant cell lines by triggering apoptosis. However, these effects are dependent on dose and there is a small difference between the dose at which selenium has a therapeutic effect and that at which it enables a toxic reaction. Chro-

nic administration of lower doses of selenium has proven to have little to no effect in this regard [4]. However, when administered with zinc, anti-carcinogenic effects are significantly boosted. This has been considered to be due to their enhancing of DNA repair mechanism and protecting the DNA from oxidative stress by inhibiting the formation of ROS. In fact, zinc deficiency was found to be linked with increased risk of cancer development in elderly population in which there were no measures of supplementation taken [5].

Although, in vitro, high levels of zinc and selenium showed to promote growth inhibition of cancer cells, therefore, halting the progression of the cancer, precautions had to be taken when administering high doses of these micronutrients. The growth inhibiting properties reflected not only on tumoral, dysplastic cells,

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but studies on rats showed decreased liver regeneration [9]. So, it was said that their effects could actually influence normal rapidly-dividing cells such as, the hepatocytes. In cancer, patients with associated liver pathologies micronutrient supplementation must be done with precaution, as it might worsen their status, even leading to liver failure, although decreasing the proliferation rate of their malignancy. Further attention must be given especially to those who presented with liver metastasis.

Pharmacokinetically speaking, zinc was thought to be particularly efficient in patients diagnosed either with benign prostate hyperplasia or prostate cancer, due to amounting to high concentrations in this organ. Therefore, zinc might be a potent therapeutic agent for decreasing the proliferation rate of the prostate cancer cells and enabling the use of less debilitating therapeutic routes and better survival chances. Zinc was also found to realize high concentrations in the liver, but as of now there are no studies indicating it to have any therapeutic benefit in liver cancer, in fact, as we stated earlier, it showed to inhibit the growth of normal liver cells [11].

A recent study showed that patients that have been recently diagnosed with prostate cancer also presented with low selenium serum levels. Thus, it was hypothesized that blood selenium levels could be not only a risk factor for certain malignancies, but also an indicator that the patient might be suffering from a cancer. Furthermore, it was found that selenium levels were also lowered in urine and correlated with a certain degree of anemia. This correlation might enable the physicians to diagnose a malignancy more rapidly, thus resulting in better survival rate for the patient [6].

Zinc and selenium levels, whether independently or combined, were also found to be a protective factor against colorectal cancer. However, this relation was found to depend on oxidative-stress gene polymorphism such as superoxide dismutase 1, superoxide dismutase 2, glutathione peroxidase and catalase. Selenium alone, proved to have antineoplastic activity, lowering the risk of colorectal cancer. On the other hand, patients with the allelic variant rs4998557 of the superoxide dismutase 1 and with adequate zinc intake were found to be at lower risk for colorectal cancer, as well. Yet zinc alone, did not showed any additional anticancerous activity, were it not correlated with this gene polymorphism or adequate selenium intake [7].

Low serum levels of selenium were associated with higher morbidity rate in patients with gastric cancers, regardless of their localization. Also, it was advised to check for both zinc and selenium levels pre-operatively and to try and manage them. Adequate serum zinc levels were correlated with better, but, not faster wound healing, however, higher levels have proven to be toxic. With regard to selenium, serum levels were highly indicative of the location of the cancer in gastric neoplasms [8].

By analyzing the serum levels of a number of metals in patients with lung cancer, it was observed that there seemed to be an association between high zinc serum levels and the incidence of this type of cancer. This was attributed to the fact that patients with high zinc levels exhibited less telomere attrition as compared with those with low levels. Yet this result was highly dependent on each patient lifestyle, being more evident in those who were not exposed to other lung cancer risk factors such as smoking or

chronic exposure to chemicals and seemed to be more frequent in males rather than females [10].

Cachexia is frequently associated with cancer and it correlates with low serum levels of proteins, as well as, micronutrients. However, studies showed that there is a strong positive correlation between zinc levels and serum albumin levels, thus leading to the conclusion that zinc supplementation might alleviate cachexia and lead to a betterment in patient nutritional status. The same correlation seemed not to apply for selenium alone, but a relation between serum zinc levels and serum selenium levels was observed [12].

## Conclusion

Zinc and selenium are two antioxidant micronutrients that have been proven to exhibit antitumoral effects by inhibiting malignant cell growth. Adequate serum levels of these two correlated with a slower progression of the cancer and a better status of the patient, resulting in better survival rates and better success rates of the therapeutic interventions. However, further studies must be done to establish exactly whether these two should be supplemented, together or alone, and to assess their toxic potential on normal organs.

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