Letter to the Editor

Selenium supplementation can relieve the clinical complications of COVID-19 and other similar viral infections

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Dear Editor,

As coronavirus infectious disease 2019 (COVID-19) is taking more and more lives around the world, scientific experts are doing their best to investigate more aspects of the disease and look for possible treatments. COVID-19 as a highly contagious RNA virus infection causes severe complications such as acute respiratory distress syndrome (ARDS), fulminant myocarditis, and systemic inflammatory response syndrome (SIRS). Besides the viral replication and the consequent cell apoptosis, the viral spike interaction with transmembrane angiotensin-converting enzyme 2 (ACE2) causes a disturbance in the angiotensin system and further deleterious oxidative damage to body tissues [1, 2].

Among many suggested treatments, the crucial role of supportive nutrient therapies is almost neglected and no definitive nutrient therapy regimens for COVID-19 patients have yet been recommended [3]. Selenium, a trace element taking part in human physiology as selenocysteine, could be a subject of interest in this era. Altogether, 25 selenocysteine containing proteins (selenoproteins) have yet been explored about half of which do not yet possess a well-described function [4]. Some of selenoproteins are more well-known including active proteins in redox homeostasis (e.g. glutathione peroxidase and thioredoxin reductase), proteins located in the endoplasmic reticulum (ER) (e.g. selenoprotein F and K), and selenium transporter in serum (selenoprotein P). Besides their antioxidant functions, glutathione peroxidase, thioredoxin reductase, and other enzymatic selenoproteins play significant roles in cell signaling pathways and gene expression of leukocytes. The selenoproteins located in ER mostly function in protein synthesis and ER stress response [5]. The efficacy of "selenium supplementation" has been studied in many conditions associated with oxidative stress and inflammatory states like cancer, autoimmune, and infectious diseases [6]. In the context of viral diseases, selenium supplementation not only could boost the immune system against the infection but also helps to neutralize the oxidative stress caused by viral pathogenesis or as a consequence of severe systemic inflammatory response [5, 7].

Clinical and experimental studies have demonstrated that selenium supplementation reinforces the oxidative defense system through enhancing the glutathione peroxidase and thioredoxin reductase activity [6]. Selenium also plays a crucial role in recycling the extra-mitochondrial coenzyme Q10 which has a prominent role in cellular oxidative defense [8].

The inhibitory effect of selenium on Transient receptor potential melastatin 2 (TRPM2) [9], a Ca^{+} channel that contributes to cell apoptosis in response to COVID-19 and other cellular oxidative stress, could also prevent cell death caused by viral replication [10] (Figure 1).

The immune-boosting mechanism of selenium supplementation contributes to increasing the number of reactive T cells, enhancing the phagocytic and migratory function of macrophages, changing macrophages tendency from pro-inflammatory to anti-inflammatory phenotypes, increasing

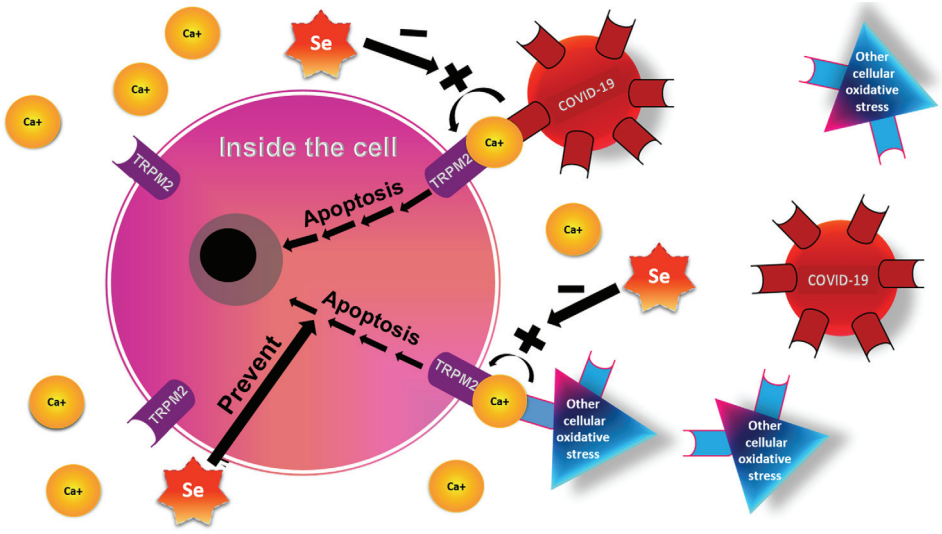

Figure 1. The inhibitory effect of selenium on Transient receptor potential melastatin 2 (TRPM2), a Ca^{+} channel that contributes to cell apoptosis in response to COVID-19 and other cellular oxidative stressors.

oxidative stress resistance in neutrophils and, enhancing the T-cell mediated antibody secretion by B-cells [5]. Moreover, the downregulating effect of selenium supplementation on NF-κβ, a pro-inflammatory transcription factor necessary for viral replication, not only ameliorates the systemic inflammatory response but also prevents viral replication and pathogenesis [11] (Figure 2). Evidence on RNA viruses like influenza and coxsackie B indicates that there is a higher probability of viral genome mutation and further risk of developing more pathogenic strains in selenium depleted hosts [7]. Regarding the prominent role of selenium in body stress response and the fact that in critically ill patients serum and tissue levels of selenium decreases, a recent meta-analysis presented that selenium supplementation in ICU patients could reduce the total mortality [12]. Meanwhile, there is limited evidence that long-term selenium supplementation can increase the risk of type 2 diabetes mellitus [13]. Thus, a general recommendation to supplement is not recommended. Although the recommended dietary allowance (RDA) for both men and women is 55 μg (0.7 μmol)/day [14], in COVID-19 patients with no kidney injury, supraphysiological doses of selenium supplementation up to 800 micrograms/day would be likely well tolerated [15] and may lower the risk of lethal complications in both hospitalized and non-hospitalized patients.

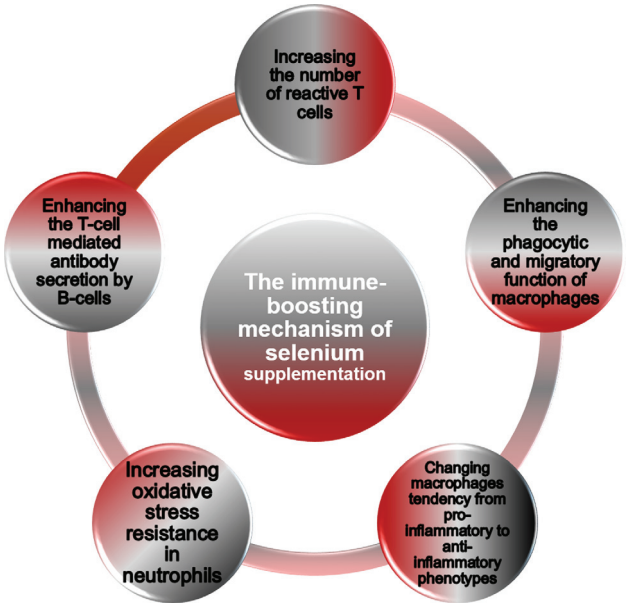

Figure 2. The immune-boosting mechanism of selenium supplementation contributes to increasing the number of reactive T cells, enhancing the phagocytic and migratory function of macrophages, changing macrophages tendency from pro-inflammatory to anti-inflammatory phenotypes, increasing oxidative stress resistance in neutrophils and, enhancing the T-cell mediated antibody secretion by B-cells.

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Conflict of interest
The authors declare that there are no conflicts of interest.

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