Review

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Review

Selenium As A Nutritional Shield in Viral Defense: A Narrative Review

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Abstract: Selenium, an essential micronutrient, plays a critical role in immune function, oxidative stress regulation, and antiviral defense. This review highlights selenium's diverse biological functions, its role in reducing oxidative stress, and its impact on immune modulation. Studies have shown that selenium enhances immune response, mitigates inflammation, and supports antiviral properties. Its deficiency is associated with increased susceptibility to viral infections, including HIV and COVID-19. The potential of selenium as a therapeutic agent in managing viral diseases and improving immune responses is discussed, emphasizing its significance in public health, particularly in selenium-deficient regions.

Keywords: Selenium; Micronutrient; Antiviral; HIV; COVID-19

1. Introduction to Selenium

Selenium is an essential micronutrient that plays a significant role in human health. Research has shown that selenium influences differential epigenetic and transcriptional regulation of genes, such as the carnitine palmitoyl transferase 1B (CPT1B) gene in obese women (1). Additionally, studies have explored the effects of exogenous selenium on promoting cadmium reduction and selenium enrichment in rice, highlighting the importance of selenium supplementation in agricultural practices (2). Furthermore, the role of selenium in enhancing nutritional substance, trace elements, and pigments in waxy maize grains through foliar application has been investigated, emphasizing the potential benefits of selenium in improving the nutritional quality of crops (3). Selenium has also been studied in the context of cancer treatment, with sodium selenite inducing autophagy and apoptosis in cervical cancer cells through the activation of specific pathways (4). Moreover, selenium distribution in serum selenoproteins has been associated with cardiovascular risk factors in healthy populations with moderate selenium levels, highlighting the importance of selenium in cardiovascular health (5). The study emphasizes the role of selenium as a trace element in various surgical morbidities, underscoring its significance in surgical practices (6).

2. Biological Significance

Selenium is a crucial element in redox biology, playing a significant role in various physiological functions. (7) highlighted the importance of selenium in antioxidant defense, hormone metabolism, DNA synthesis, and repair, emphasizing its role in maintaining cellular redox status and genetic stability. Selenium functions as a cofactor in selenoproteins, contributing to their antioxidant and immune-regulatory roles. (8) demonstrated that selenium reduces ubiquinone via sulfide quinone oxidoreductase, suppressing ferroptosis and expanding our understanding of selenium's regulatory mechanisms. Furthermore, (9) proposed the Selenium-SelK-GPX4 axis as a protective mechanism against ferroptosis and cellular senescence, highlighting the importance of selenium in cellular homeostasis. In addition to its antioxidant functions, selenium has been implicated in various health

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conditions. One study showed that selenium nanoparticles can ameliorate lumbar disc degeneration by restoring redox homeostasis and mitochondrial function in nucleus pulposus cells (10). Furthermore, the role of selenoprotein W in regulating CD4+ T cell differentiation was investigated in selenium-deficient chicken spleens, highlighting the impact of selenium deficiency on immune responses (11).

3. Selenium and Oxidative Stress

Selenium, a trace element, plays a crucial role in reducing oxidative stress through the activity of specific selenocysteine-containing proteins such as glutathione peroxidase and thioredoxin reductase. These proteins are essential components of the antioxidant defense system, contributing to the maintenance of redox homeostasis in various physiological processes. (12) highlighted the detrimental effects of oxidative stress in pregnancy, emphasizing the importance of understanding mechanisms to mitigate its impact. Animal models have been instrumental in studying the role of selenium in oxidative stress-related conditions due to limitations in conducting experimental studies on pregnant women. Another study discussed the significance of selenocysteine-containing proteins, including glutathione peroxidases and thioredoxin reductases, in redox biology (13). These proteins demonstrate selenium's essential role in physiological functions and its advantage over sulfur in certain functional proteins. Studies have highlighted the role of selenium in redox regulation, particularly in controlling NOD-like receptor protein 3 (NLRP3)-mediated inflammation and pyroptosis (14). Glutathione peroxidase and thioredoxin reductase, containing selenocysteine residues, play a crucial role in suppressing oxidative stress and regulating inflammatory processes. One study underscored the critical role of selenoproteins, such as glutathione peroxidase and thioredoxin reductase, in cardiovascular redox homeostasis (15). These selenoproteins serve as enzymatic antioxidants, providing a first-line defense against oxidative stress in the heart. The review highlighted the therapeutic potential of selenoproteins in cardiovascular pathophysiology, calling for more detailed clinical studies to explore their benefits further.

4. Impact on the Immune System

Selenium, an essential trace element, plays a pivotal role in enhancing both innate and adaptive immunity through its incorporation into selenoproteins, which regulate oxidative stress and immune cell functions. Recent studies have provided insights into various immune mechanisms, where selenium's role could intersect. For instance, discussed the crosstalk between Retinoic acid-related orphan receptor gamma t (RORγt) group 3 innate lymphoid cells (ILC3s) and adaptive immune responses in mucosal and lymphoid tissues, highlighting their significance in immune regulation (16). Selenium, by reducing oxidative stress and promoting the activity of immune cells such as ILC3s, could further enhance these interactions. Similarly, another study explored programmed cell death (PCD) pathways, including apoptosis, pyroptosis, and ferroptosis, which are influenced by redox balance (17). Selenium's antioxidant properties may mitigate excessive oxidative stress, thereby modulating PCD and improving immune responses in cancer therapy.

One study examined the Aryl Hydrocarbon Receptor-Interacting Protein's (AIP) role in cancer and immunity, suggesting functions beyond its chaperone activity (18). While selenium's direct connection to AIP remains unexplored, its involvement in oxidative stress regulation and immune modulation could intersect with AIP-associated pathways in cancer. Moreover, highlighted the role of gut microbiota in modulating immunity through metabolites like tryptophan derivatives and short-chain fatty acids, which influence dendritic cells, macrophages, and CD4 T cells (19). Selenium may support these processes by maintaining mucosal integrity and strengthening gut-associated lymphoid tissue immunity.

Another study explored how the Cyclic GMP-AMP Synthase-Stimulator of Interferon Genes (cGAS-STING) pathway remodels the tumor microenvironment to enhance immunotherapy outcomes, a process where selenium could modulate inflammation and oxidative stress to improve

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therapy efficacy (20). A study further emphasized the role of natural killer (NK) cells in bridging innate and adaptive immunity against hepatocellular carcinoma, proposing strategies to restore Natural Killer Group 2, Member D (NKG2D) signaling (21). Selenium's role in supporting NK cell cytotoxicity and reducing inflammation may complement such immunotherapeutic approaches.

5. Antiviral Properties of Selenoproteins

Selenium, a crucial component of selenoproteins and selenocompounds in the human body, has been shown to play a significant role in various physiological processes. One such area of interest is selenium's potential antiviral activity through selenoprotein-mediated mechanisms (22). Studies have indicated that increased dietary selenium consumption can enhance the antioxidant activity of glutathione peroxidase (GPx), which in turn can improve male fertility and aid in maintaining sperm integrity (22). Furthermore, selenium nanoparticles synthesized through biological processes have shown promise in biomedical applications, highlighting the diverse roles selenium can play in antiviral defense mechanisms (23). Research has also explored the immunomodulatory effects of selenium, with evidence pointing towards the role of selenoproteins such as selenoprotein K (SelK) in regulating the immune system (24). Additionally, studies have demonstrated the antiviral activity of selenium, with selenium nanoparticles inhibiting apoptosis and showing therapeutic potential against influenza A virus (25). The association between regional selenium status and reported viral infections further supports the antiviral effects of selenium, suggesting that selenium may act through multiple cellular and viral mechanisms to combat viral infections (26). Overall, the literature reviewed provides compelling evidence of selenium's antiviral properties through selenoprotein-mediated mechanisms. From enhancing antioxidant activity to modulating the immune system, selenium's role in antiviral defense mechanisms is a promising area of research that warrants further exploration.

6. Selenium Deficiency and Viral Susceptibility

Selenium is an essential micronutrient that plays a crucial role in immune function. Studies have shown that selenium deficiency is associated with increased vulnerability to viral infections (27). In individuals with HIV, selenium deficiency has been linked to a higher risk of morbidity and mortality, highlighting the importance of adequate selenium levels in immune health (28). Additionally, low selenium status is common in certain regions, such as the United States and Canada, and can impair immune function, leading to increased susceptibility to infections (29). Malnutrition, including deficiencies in essential nutrients like selenium, can compromise immune response and increase susceptibility to infections (30). Individuals with compromised immune systems, such as those with IgG2 subclass deficiency, are more susceptible to complications from common infections, including viral and bacterial gastrointestinal (GI) infections (31). Furthermore, selenium deficiency has been associated with Keshan Disease, a condition characterized by viral and fungal infections, highlighting the importance of selenium in immune health (32). Overall, maintaining adequate selenium levels is crucial for immune function and reducing vulnerability to viral infections. Further research is needed to explore the mechanisms by which selenium deficiency increases susceptibility to infections and to develop strategies to address this issue (33). By understanding the role of selenium in immune health, healthcare professionals can better support individuals in maintaining optimal selenium levels to enhance their immune response and reduce the risk of viral infections (34).

7. Selenium and Viral Mutation

Selenium is a crucial element that has been studied for its potential role in viral mutation and disease. Fabian et al. (2024) investigated Selenium deficiency has been associated with Keshan Disease (KD), a condition with potential etiological factors including genetic predispositions, viral infections, and malnutrition. Furthermore, Zhang et al.(2020) informed selenium status has been

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linked to increased viral replication and mutation rates, as well as higher pathogenicity or mortality under selenium deficiency. Research has also explored the use of selenium compounds as antiviral agents, showing promise in the treatment of viral diseases at different stages due to the high genetic diversity and mutation rates of viruses (35). Guo et al. investigated selenium nanoparticles for their therapeutic potential in inhibiting apoptosis and controlling viral mutations, particularly in the context of influenza virus mutations. Moreover, Sadler et al.(2024) observed inadequate selenium intake has been linked to adverse health events, including increases in cancer incidence and pathogenic viral mutations. This highlights the importance of selenium in modulating the immune response and potentially influencing viral mutation rates. Overall, the literature suggests that selenium plays a significant role in viral mutation and disease, with implications for antiviral strategies and understanding the genetic and immunological aspects of viral infections.

8. HIV and Selenium

The role of selenium in various biological processes and its potential biomedical applications have been extensively studied. According to Mikhailova (2023), selenium nanoparticles exhibit antimicrobial, antiviral, anticancer, antioxidant, and anti-inflammatory properties, positioning them as promising candidates for therapeutic interventions. The bioavailability of selenium nanoparticles is influenced by their amorphous structure and crystal stability, which determine their efficacy in biological systems (36). Maia et al. (2023) highlight that selenium is not simply a fortuitous substitute for sulfur in redox biology but plays critical roles in antioxidant defense, hormone metabolism, DNA synthesis and repair, and overall human health. In the context of HIV treatment, selenium-based compounds have shown anti-HIV activity, highlighting the potential of selenium in combating the virus (37). Additionally, selenium supplementation has been studied in HIV-infected individuals, showing changes in body composition and gene expression related to immune function (38). Micronutrient supplementation, including selenium, has been investigated for its impact on clinical outcomes in adults living with HIV on antiretroviral therapy, emphasizing the importance of adequate nutrient intake in managing HIV (39). Furthermore, surface modification of nanomaterials with selenium has been explored for enhanced drug delivery in HIV treatment, showcasing the potential of selenium-based materials in improving therapeutic outcomes (40). Overall, selenium's diverse properties and roles in biological systems make it a promising avenue for further research in the context of HIV treatment and overall health.

9. SARS-CoV-2 and Selenium

Selenium is a micronutrient that plays a crucial role in immunity and has been studied for its potential anti-viral activity, particularly against SARS-CoV-2. The mechanism of the antiviral activity of a novel hydroponically selenium-enriched garlic powder against SARS-CoV-2 replication was investigated (41). Additionally, Leveraging SARS-CoV-2 Main Protease (Mpro) for COVID-19 mitigation with selenium-based inhibitors has been explored (42). This highlights the potential of selenium-containing drugs in combating COVID-19. Additionally, a study examined the associations between micronutrients and antibody responses in individuals vaccinated with an inactivated COVID-19 vaccine (43). The findings suggest that micronutrients, including selenium, may have an impact on humoral responses to vaccination. Additionally, dietary supplements containing selenium have been investigated for their potential antiviral, anti-inflammatory, and immune-enhancing effects (44). Research has also shown that selenium deficiency in COVID-19 patients may be associated with worse disease outcomes (45). This underscores the importance of maintaining adequate selenium levels for optimal immune function. Moreover, Zhang (2020) investigated the relationship between regional selenium status and reported COVID-19 cases, highlighting a potential link between selenium deficiency and disease prevalence.

10. Influenza and Selenium

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Recent research has shown that nanoparticles made from selenium have demonstrated significant antiviral capacity against the influenza A virus (46). Additionally, Jain et al. (2024) indicated that selenium deficiency is associated with the pathogenicity of various viruses, including influenza. Furthermore, Guo et al. (2024) demonstrated that selenium inhibits apoptosis and inflammation in cells infected with the H1N1 influenza A virus, indicating its potential as a therapeutic agent. This aligns with evidence highlighting selenium as an essential trace element with notable antiviral properties. Moreover, selenium has been linked to the prevention of viral infections, including influenza viruses, hepatitis B virus, and coronaviruses (47). Selenium deficiency has been shown to inhibit T cell immunity, which can promote the replication of the influenza virus (48). Selenium nanoparticles have emerged as a promising strategy for combating the influenza virus, and further research in this area could lead to the development of effective antiviral treatments (49).

11. Selenium-Enriched Foods

Selenium is an essential mineral that plays a crucial role in immune function and antiviral defense. As per Health Professional Fact Sheet (2024) Selenium-rich foods such as Brazil nuts, fish, and cereals are important dietary sources of this micronutrient. Brazil nuts, in particular, are highlighted as a potent source of selenium, with just one nut a day being sufficient to meet daily selenium needs (50). Sadler et al. (2024) expressed other sources of selenium include dairy products, meat, breads, nuts, and mushrooms. The amount of selenium in food can vary depending on the geographical area where the product is grown, emphasizing the importance of diverse dietary sources (51). In addition to its role in antiviral defense, selenium has been shown to reduce inflammation, lower cancer risk, and impact thyroid function (52). A daily intake of 50 mcg of selenium is recommended to maintain these functions (52). Fish, such as tuna and shrimp, are also highlighted as nutrient-dense sources of selenium (53). Furthermore, selenium has been identified as a potential source of antiviral agents, further underscoring its importance in immune function (54). Overall, selenium-enriched foods like Brazil nuts, fish, and cereals play a significant role in supporting antiviral defense and overall immune function. Including these foods in the diet can help ensure an adequate intake of selenium, which is essential for maintaining optimal health and well-being (55).

12. Supplementation Strategies

Selenium is a trace mineral that has been studied for its potential benefits in antiviral purposes. Mitochondrial dysfunction and Coenzyme Q10 supplementation have been suggested as potential benefits for COVID-19 infection (56). Additionally, Osuna-Padilla et al. (2024) reported that zinc and selenium supplementation demonstrated potential clinical and immunological benefits in individuals with HIV. While selenium is essential for plant growth and development, its dynamics in plants are influenced by various factors such as soil conditions and microorganisms (57,58). This highlights the importance of understanding the role of selenium supplementation in antiviral strategies. In the context of micronutrient supplementation for immune support, various nutritional agents have been identified for their ability to reduce the risk of infection and attenuate immune changes (59). This suggests that selenium supplementation may play a role in supporting immune function for antiviral purposes. Overall, while selenium supplementation has shown potential benefits in various contexts, it is important to consider the dosage and exposure times to ensure that the benefits outweigh the risks (60).

13. Selenium Toxicity

Selenium is an essential mineral that plays a crucial role in various bodily functions. According to the Selenium Health Professional Fact Sheet, while selenium is essential for maintaining good health, excessive intake can result in toxicity and negative health effects. Symptoms of selenium toxicity can include hair loss, digestive problems, and even mild nerve damage (61). Selenosis, or

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selenium toxicity, is rare in the United States but can occur with excessive consumption (62). Excessive intake of selenium can have serious health implications. Sadler et al. (2024) highlighted the immunomodulatory effects of selenium, noting that while its benefits have been studied, excessive intake whether in organic or inorganic form can be detrimental to human health. Indeed, symptoms of selenium toxicity include a range of adverse health conditions (63). It is important to be aware of the risks associated with excessive selenium intake. While selenium is necessary for good health in appropriate amounts, it can be toxic in excessive amounts (64). The Selenium Health Professional Fact Sheet states that the tolerable upper intake level (UL) for selenium represents the maximum daily amount that can be consumed without risking adverse health effects. Therefore, it is crucial to be mindful of selenium intake levels to avoid potential health risks associated with toxicity. Flowers-Kelvin (2024) emphasized the importance of recognizing the signs and symptoms of selenium toxicity and monitoring intake levels to mitigate potential health risks.

14. Selenium in Animal Models

Selenium is a crucial element that plays a significant role in various biological processes, including immune response and antioxidant defense mechanisms. Several studies have explored the impact of selenium on viral infections and supplementation in animal models. The virulence of Coxsackievirus B6 strains and the efficacy of antiviral treatments were investigated in a neonatal murine model, underscoring the importance of studying virus-host interactions (65). Selenium deficiency has been shown to exacerbate Bisphenol A-induced intestinal toxicity in chickens, highlighting selenium's crucial role in mitigating such toxic effects (66). The protective effects of functional nano-selenium supplementation on spleen injury were explored, revealing its role in regulating specific protein expressions and highlighting the potential benefits of selenium supplementation in preventing organ damage (67). Additionally, it was found that selenium mitigated lead-induced neurotoxicity in chickens by modulating specific pathways, suggesting its potential therapeutic role in reducing toxic effects (68). Furthermore, the antiviral potential of oreochromicin-1 was investigated against a broad range of animal viruses, providing valuable insights into the development of novel antiviral drugs (69). The effect of selenium nanoparticles on lipid profiles in lambs was studied, suggesting a potential role for selenium in improving lipid profiles (70).

15. Selenium and Antiviral Drug Synergy

Selenium is a trace element that has been studied for its potential interactions with antiviral drugs to enhance efficacy. While the provided documents do not directly address this specific topic, they shed light on various aspects of antiviral drug development and potential targets for antiviral therapy. The role of catechol-O-methyltransferase (COMT) in glioma treatment was explored, demonstrating how targeting this enzyme can sensitize glioma to radiotherapy (71). This study highlights the importance of identifying novel drug targets to enhance the efficacy of existing treatment modalities. The potential targets of Astragalus in liver cancer were investigated using network pharmacology, highlighting the importance of understanding the molecular mechanisms underlying the therapeutic effects of natural compounds (72). This approach could be applied to study the interactions between selenium and antiviral drugs to identify synergistic effects. A study identified naturally derived terpenoids with antiviral activity against the Foot-and-Mouth Disease Virus, highlighting the potential of secondary metabolites as effective antiviral agents (73). Selenium, known for its antioxidant properties, could potentially enhance the antiviral effects of such compounds. Similarly, another study discovered two novel compounds that inhibit Flavivirus infection by targeting lipid metabolism (74). Selenium, with its role in antioxidant defense and immune function, could potentially interact with lipid metabolism pathways to enhance the antiviral activity of these compounds. While the provided documents do not directly address selenium's

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interactions with antiviral drugs, they offer valuable insights into antiviral drug development, potential drug targets, and using natural compounds for antiviral therapy.

16. Geographic Variation and Deficiency

The Selenium Health Professional Fact Sheet states that selenium deficiency is associated with an increased prevalence of various health conditions, including thyroid disease. Fabian et al. (2024) state that regions with low selenium intake exhibit a higher incidence of certain diseases, such as Keshan disease, linked to selenium deficiency and viral infections. Additionally, environmental factors, such as deficiencies in vitamins and minerals like vitamin A and selenium, have been implicated in the development of esophageal cancer in specific geographic areas (75). Furthermore, Morales et al. (2023) state that malnutrition and deficiencies in essential nutrients can compromise the immune response, increasing susceptibility to infections. Another study by Sadler et al. (2024) observed that in regions where selenium deficiency is prevalent, individuals tend to have lower plasma selenium levels, which increases their susceptibility to viral infections. This is particularly relevant, as Fabian et al. (2024) note that in areas where Keshan disease is endemic, selenium deficiency is associated with an increased risk of viral infections. The impact of environmental factors, including selenium deficiency, on the development of various health conditions has been well-documented. For example, iodine intake, vitamin D deficiency, and viral infections have all been associated with an increased risk of certain diseases (76). In regions where selenium deficiency is common, individuals may be more susceptible to viral infections caused by pathogens like Epstein–Barr Virus and Human Parvovirus B19 (76).

17. Role in Cytokine Regulation

Selenium is known to play a crucial role in controlling the production of pro- and anti-inflammatory cytokines. A study by Sadler et al. (2024) has shown that selenium promotes the differentiation of pro-inflammatory M1 macrophages to anti-inflammatory M2 macrophages, highlighting its immunomodulatory effects. Additionally, selenium nanoparticles synthesized from Nelumbo nucifera have been found to modulate the expression of pro- and anti-inflammatory cytokines in response to bacterial infection-induced immune-antioxidant suppression (77). Furthermore, the impact of selenium on cytokine production has been studied in the context of various diseases. For instance, in multiple sclerosis (MS), targeting dopaminergic receptors has been shown to have both pro- and anti-inflammatory effects on monocytes and macrophages, suggesting a potential role for selenium in immunomodulation in MS (78). Additionally, dietary biogenic selenium nanoparticles have been found to improve growth and reduce inflammation by modulating the production of pro-inflammatory cytokines (79).

18. Public Health Implications

Selenium is a micronutrient that has been shown to play a crucial role in promoting apoptosis, which is essential for preventing unchecked cell proliferation in cancer (80). Additionally, Morales et al. (2023) observed that selenium is linked to improved immune function and resistance to infections, suggesting its potential to enhance viral resistance at the population level. Furthermore, cellular zinc metabolism has been found to enhance resistance and combat oxidative stress, indicating the importance of micronutrients like selenium in improving overall health and immunity (81). Studies have also shown that selenium levels can impact viral infections, with research indicating that selenium supplementation may reduce viral RNA levels and improve viral resistance (82). Moreover, Huang et al. (2024) explain that selenium is suggested to have a positive effect on immunity and stress resistance, highlighting its potential to improve population-level viral resistance. According to the Health Professional Fact Sheet (2024), in the context of COVID-19, selenium has been identified as a potential dietary supplement that may help lower viral replication rates and suppress inflammation, further emphasizing its role in enhancing viral resistance. Overall, improving selenium status in

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populations, particularly in regions like Southern Africa where selenium deficiency is prevalent, may have significant benefits in enhancing viral resistance and overall health (83).

19. Future Directions

Selenium is a mineral that plays a crucial role in various bodily functions, including immune function. The Selenium Health Professional Fact Sheet states that selenium supplementation may benefit individuals with HIV, but further studies are needed to determine the extent of these benefits. Huang (2024) noted that in the context of the COVID-19 pandemic, nanotechnology has emerged as a frontier in combatting infectious and inflammatory diseases, including potential applications for selenium-based treatments. According to the Health Professional Fact Sheet, while other dietary supplement ingredients, such as botanicals and probiotics, may influence immune function, selenium stands out for its critical and essential role in the body. In the treatment of HIV/AIDS, a combination of anti-HIV medicines from different classes is typically used to manage the disease (84). The HIV pandemic has led to increased infections of true pathogens in certain fungi, highlighting the importance of continued research in this area (85). Additionally, exploring the link between oxidative stress, selenium levels, and COVID-19 outcomes may provide valuable insights into the potential benefits of selenium supplementation in managing the disease (86). As research continues to evolve, future studies should focus on the long-term effects of nutritional interventions, particularly in the context of post-COVID recovery (87). Understanding the interactions between drugs, nutrition, and infectious diseases like COVID-19 is essential for developing effective treatment strategies (88). Moving forward, research priorities should include investigating the impact of selenium on immune function in individuals with HIV and COVID-19, as well as exploring potential synergies between selenium supplementation and other treatment modalities.

20. Conclusion

Selenium is a vital trace element with significant antiviral, antioxidant, and immune-modulatory properties. Its deficiency is linked to increased susceptibility to viral infections and various health conditions. Supplementing selenium has shown promise in improving immune function and reducing viral replication, especially in diseases like HIV and COVID-19. Future research should focus on better understanding selenium's mechanisms, its clinical efficacy in diverse disease contexts, and its potential as a therapeutic agent to enhance global health.

References

1. Watanabe LM, Pereira VA, Noronha NY, de Souza Pinhel MA, Wolf LS, de Oliveira CC, Plaça JR, Noma IH, da Silva Rodrigues G, de Souza VC, Júnior FB. The influence of serum selenium in differential epigenetic and transcriptional regulation of CPT1B gene in women with obesity. Journal of Trace Elements in Medicine and Biology. 2024 May 1;83:127376.
2. Huang F, Chen L, Zhou Y, Huang J, Wu F, Hu Q, Chang N, Qiu T, Zeng Y, He H, White JC. Exogenous selenium promotes cadmium reduction and selenium enrichment in rice: Evidence, mechanisms, and perspectives. Journal of Hazardous Materials. 2024 Jun 26:135043.
3. Lu B, An H, Song X, Yang B, Jian Z, Cui F, Xue J, Gao Z, Du T. Enhancement of Nutritional Substance, Trace Elements, and Pigments in Waxy Maize Grains through Foliar Application of Selenite. Foods. 2024 Apr 26;13(9):1337.
4. Lv C, Zeng Q, Qi L, Wang Y, Li J, Sun H, Du L, Hao S, Li G, Feng C, Zhang Y. Sodium Selenite Induces Autophagy and Apoptosis in Cervical Cancer Cells via Mitochondrial ROS-Activated AMPK/mTOR/FOXO3a Pathway. Antioxidants. 2024 Aug 19;13(8):1004.
5. Letsiou S, Damigou E, Nomikos T, Pergantis SA, Pitsavos C, Panagiotakos D, Antonopoulou S. Deciphering the associations of selenium distribution in serum GPx-3 and selenoprotein P with cardiovascular risk factors in a healthy population with moderate levels of selenium: The ATTICA study. Journal of Trace Elements in Medicine and Biology. 2024 Dec 1;86:127509.

 doi:10.20944/preprints202502.2251.v1

6. Alarfaj H. Selenium in Surgery. Cureus. 2024 Oct 22;16(10):e72168.
7. Maia LB, Maiti BK, Moura I, Moura JJ. Selenium—more than just a fortuitous sulfur substitute in redox biology. Molecules. 2023 Dec 24;29(1):120.
8. Lee N, Park SJ, Lange M, Tseyang T, Doshi MB, Kim TY, Song Y, Kim DI, Greer PL, Olzmann JA, Spinelli JB. Selenium reduction of ubiquinone via SQOR suppresses ferroptosis. Nature Metabolism. 2024 Feb;6(2):343-58
9. Jia C, Xiang Z, Zhang P, Liu L, Zhu X, Yu R, Liu Z, Wang S, Liu K, Wang Z, Vasilev K. Selenium-SelK-GPX4 axis protects nucleus pulposus cells against mechanical overloading-induced ferroptosis and attenuates senescence of intervertebral disc. Cellular and Molecular Life Sciences. 2024 Dec;81(1):49.
10. He W, Tian X, Zhou Q, Lv J, Li Y, Jin C, Liu H, Yang H, Xu Y, He F, Liu T. Selenium nanoparticles ameliorate lumbar disc degeneration by restoring GPX1-mediated redox homeostasis and mitochondrial function of nucleus pulposus cells. Journal of Nanobiotechnology. 2024 Oct 18;22(1):634.
11. Wang X, Ding J, Chen K, Hu H, Huang B, Shi G, Li S. Probing Selenium-Deficient Chicken Spleen Th1/Th17 Differentiation Based on Selenoprotein W Targeting of PKM2/HIF1α. Journal of Agricultural and Food Chemistry. 2024 Nov 6.
12. Grzeszczak K, Łanocha-Arendarczyk N, Malinowski W, Ziętek P, Kosik-Bogacka D. Oxidative stress in pregnancy. Biomolecules. 2023 Dec 9;13(12):1768.
13. Chaudière J. Biological and catalytic properties of selenoproteins. International Journal of Molecular Sciences. 2023 Jun 14;24(12):10109.
14. Rusetskaya NY, Loginova NY, Pokrovskaya EP, Titova LE. Redox regulation of the NLRP3-mediated inflammation and pyroptosis. Biomeditsinskaya khimiya. 2023 Dec 25;69(6):333-52.
15. Angelone T, Rocca C, Lionetti V, Penna C, Pagliaro P. Expanding the frontiers of guardian antioxidant selenoproteins in cardiovascular pathophysiology. Antioxidants & Redox Signaling. 2024 Mar 1;40(7-9):369-432.
16. Wang W, Li N, Guo X. The crosstalk between ILC3s and adaptive immunity in diseases. The FEBS Journal. 2024 Sep;291(18):3965-77.
17. Wang M, Yu F, Zhang Y, Li P. Programmed cell death in tumor immunity: mechanistic insights and clinical implications. Frontiers in Immunology. 2024 Jan 12;14:1309635.
18. Kazzaz SA, Tawil J, Harhaj EW. The Aryl Hydrocarbon Receptor Interacting Protein in cancer and immunity: Beyond a chaperone protein for the dioxin receptor. Journal of Biological Chemistry. 2024 Mar 11:107157.
19. Yu YJ, Liu XD, Liao C, Yu R, Wang X, Li M, Wang Y. Targeting gut microbiota for immunotherapy of diseases. Archives of Toxicology. 2024 May 9:1-1.
20. Huang M, Cha Z, Liu R, Lin M, Gafoor NA, Kong T, Ge F, Chen W. Enhancing immunotherapy outcomes by targeted remodeling of the tumor microenvironment via combined cGAS-STING pathway strategies. Frontiers in Immunology. 2024 May 16;15:1399926.
21. Shin SK, Oh S, Chun SK, Ahn MJ, Lee SM, Kim K, Kang H, Lee J, Shin SP, Lee J, Jung YK. Immune signature and therapeutic approach of natural killer cell in chronic liver disease and hepatocellular carcinoma. Journal of Gastroenterology and Hepatology. 2024.
22. Yuan S, Zhang Y, Dong PY, Yan YM, Liu J, Zhang BQ, Chen MM, Zhang SE, Zhang XF. A comprehensive review on potential role of selenium, selenoproteins and selenium nanoparticles in male fertility. Heliyon. 2024 Jul 19.
23. Mikhailova EO. Selenium nanoparticles: green synthesis and biomedical application. Molecules. 2023 Dec 15;28(24):8125.
24. Sadler RA, Mallard BA, Shandilya UK, Hachemi MA, Karrow NA. The Immunomodulatory Effects of Selenium: A Journey from the Environment to the Human Immune System. Nutrients. 2024 Sep 30;16(19):3324.
25. Guo M, Ye YD, Cai JP, Xu HT, Wei W, Sun JY, Wang CY, Wang CB, Li YH, Zhu B. PEG-SeNPs as therapeutic agents inhibiting apoptosis and inflammation of cells infected with H1N1 influenza A virus. Scientific Reports. 2024 Sep 12;14(1):21318.

 doi:10.20944/preprints202502.2251.v1

26. Zhang J, Taylor EW, Bennett K, Saad R, Rayman MP. Association between regional selenium status and reported outcome of COVID-19 cases in China. The American journal of clinical nutrition. 2020 Jun 1;111(6):1297-9.
27. Palmer AC, Bedsaul-Fryer JR, Stephensen CB. Interactions of Nutrition and Infection: The Role of Micronutrient Deficiencies in the Immune Response to Pathogens and Implications for Child Health. Annual Review of Nutrition. 2024 May 9;44.
28. Health Professional Fact Sheet [Internet]. Office of Dietary Supplements - Selenium. Available from: https://ods.od.nih.gov/factsheets/Selenium-HealthProfessional/
29. Health Professional Fact Sheet [Internet]. [cited 2024 Dec 8]. Office of Dietary Supplements - Dietary Supplements in the Time of COVID-19. Available from: https://ods.od.nih.gov/factsheets/COVID19-HealthProfessional/
30. Morales F, Montserrat-de la Paz S, Leon MJ, Rivero-Pino F. Effects of malnutrition on the immune system and infection and the role of nutritional strategies regarding improvements in children's health status: A literature review. Nutrients. 2023 Dec 19;16(1):1.
31. Bula-Rudas M FAAP Fernando J. Medscape. [cited 2024 Dec 8]. Infections in the Immunocompromised Host: Practice Essentials, The Child with Frequent Infections, Immunocompromising Conditions. Available from: https://emedicine.medscape.com/article/973120-overview
32. Fabian D, Ahmed I. Keshan Disease. StatPearls. 2024 May 7;
33. Couto RD, Dos Santos DG, Sanine PR, Pires dos Santos A, Kmetiuk LB, Biondo AW, Boing AC. Mapping vulnerability for increased COVID-19 susceptibility and worse outcomes: a scoping review. Frontiers in Public Health. 2024 Oct 10;12:1432370.
34. MedlinePlus [Internet]. [cited 2024 Dec 8]. Immune System and Disorders. Available from: https://medlineplus.gov/immunesystemanddisorders.html
35. Jain VK, Priyadarsini KI. Selenium compounds as promising antiviral agents. New Journal of Chemistry. 2024;48(15):6534-52.
36. Li K, Li J, Zhang S, Zhang J, Xu Q, Xu Z, Guo Y. Amorphous structure and crystal stability determine the bioavailability of selenium nanoparticles. Journal of Hazardous Materials. 2024 Mar 5;465:133287.
37. Shi D, Xu S, Ding D, Tang K, Zhou Y, Jiang X, Wang S, Liu X, Zhan P. Advances in drug structure-activity-relationships for the development of selenium-based compounds against HIV. Expert Opinion on Drug Discovery. 2024 Feb 1;19(2):139-46.
38. Osuna-Padilla IA, Rodríguez-Moguel NC, Aguilar-Vargas A, Tolentino-Dolores M, Perichart-Perera O, Ahumada-Topete V, Ávila-Ríos S, Soto-Nava M, Diaz-Rivera D, De León-Lara E, Wilson-Verdugo M. Zinc and selenium supplementation on treated HIV-infected individuals induces changes in body composition and on the expression of genes responsible of naïve CD8+ T cells function. Frontiers in Nutrition. 2024 Sep 16;11:1417975.
39. Okoka EM, Kuyebi MA, Oyadiran OT, Okusanya TR, Onaku E, Omotayo MO, Abioye AI. Effect of Micronutrients on HIV-Related Clinical Outcomes Among Adults Living With HIV on Antiretroviral Therapy: Systematic Review and Meta-analysis. Nutrition Reviews. 2024 Nov 22:nuae171.
40. Akor FO, Edo GD, Nelson FA, Johnson AU, Iyam SO, Abubakar MN, Gulack AO, Ubah CB, Ekpong BO, Benjamin I. Surface modification of graphene and fullerene with Sulfur (S), Selenium (Se), and Oxygen (O): DFT Simulation for enhanced zidovudine delivery in HIV treatment. BMC chemistry. 2024 Aug 27;18(1):156.
41. Majeed M, Nagabhushanam K, Lawrence L, Prakasan P, Mundkur L. The Mechanism of Anti-Viral Activity of a Novel, Hydroponically Selenium-Enriched Garlic Powder (SelenoForce®) Against SARS-CoV-2 Virus. Global Advances in Integrative Medicine and Health. 2024 Jul 24;13:27536130241268100.
42. De Luca V, Angeli A, Nocentini A, Gratteri P, Pratesi S, Tanini D, Carginale V, Capperucci A, Supuran CT, Capasso C. Leveraging SARS-CoV-2 Main Protease (Mpro) for COVID-19 Mitigation with Selenium-Based Inhibitors. International Journal of Molecular Sciences. 2024 Jan 12;25(2):971.
43. Meng H, Wang Y, Zhai Y, Luo W, Wang Y, Hu Y, Liu S, Xiao W, Yang G, Ye F, Chen S. Unveiling the micronutrient-immunity puzzle in inactivated COVID-19 vaccination: A comprehensive analysis of

 doi:10.20944/preprints202502.2251.v1

circulating micronutrient levels and humoral responses in healthy adults. Journal of Medical Virology. 2024 Apr;96(4):e29611.

44. Health Professional Fact Sheet [Internet]. [cited 2024 Dec 9]. Office of Dietary Supplements - Dietary Supplements in the Time of COVID-19. Available from: https://ods.od.nih.gov/factsheets/COVID19-HealthProfessional/
45. Schaefer J, Khanna D. Nutritional and wellness strategies for neurological and psychiatric recovery from post-COVID syndrome and post-acute sequelae of COVID-19. Cureus. 2023 Dec;15(12).
46. Rios-Ibarra CP, Salinas-Santander M, Orozco-Nunnelly DA, Bravo-Madrigal J. Nanoparticle-based antiviral strategies to combat the influenza virus. Biomedical Reports. 2024 Feb 21;20(4):65.
47. Deng W, Meng C, Liu K. The association between blood selenium levels and the prevalence of herpes simplex virus in US adults: data from National Health and Nutrition Examination Survey (NHANES) 2011-2016.
48. Xu S, Wang D, Zhao W, Wei Q, Tong Y. Non-negligible role of trace elements in influenza virus infection. Metabolites. 2023 Jan 26;13(2):184.
49. Bufan B, Arsenović-Ranin N, Živković I, Ćuruvija I, Blagojević V, Dragačević L, Kovačević A, Kotur-Stevuljević J, Leposavić G. Modulation of T-cell-dependent humoral immune response to influenza vaccine by multiple antioxidant/immunomodulatory micronutrient supplementation. Vaccines. 2024 Jul 4;12(7):743.
50. Complementary Treatments :: New Zealand Herpes Foundation [Internet]. [cited 2024 Dec 9]. Available from: https://www.herpes.org.nz/living-with-herpes/complementary-treatments
51. Jarmakiewicz-Czaja S, Ferenc K, Sokal-Dembowska A, Filip R. Nutritional Support: The Use of Antioxidants in Inflammatory Bowel Disease. International Journal of Molecular Sciences. 2024 Apr 16;25(8):4390.
52. Mazmanyan V, Gasparyan A. Selenium — Sources, Health Benefits, Deficiency, and Side Effects. Food Struct [Internet]. 2024 Apr 1 [cited 2024 Dec 9]; Available from: https://foodstruct.com/articles/selenium
53. Rayman MP. The importance of selenium to human health. The lancet. 2000 Jul 15;356(9225):233-41.
54. Sarmento TC, Ferreira RD, Franco OL. Plant-Based Diet and Sports Performance. ACS Omega. 2024 Nov 6.
55. Rani J, Saini S, Jain H. Health and Nutritional Benefits Provided by Superfoods: A Review. Int. J. Curr. Microbiol. App. Sci. 2024;13(07):106-32.
56. Mantle D, Hargreaves IP, Domingo JC, Castro-Marrero J. Mitochondrial dysfunction and coenzyme Q10 supplementation in post-viral fatigue syndrome: an overview. International Journal of Molecular Sciences. 2024 Jan 1;25(1):574.
57. Hasanuzzaman M, Bhuyan MB, Raza A, Hawrylak-Nowak B, Matraszek-Gawron R, Nahar K, Fujita M. Selenium toxicity in plants and environment: biogeochemistry and remediation possibilities. Plants. 2020 Dec 4;9(12):1711.
58. Somagattu P, Chinnannan K, Yammanuru H, Reddy UK, Nimmakayala P. Selenium dynamics in plants: Uptake, transport, toxicity, and sustainable management strategies. Science of The Total Environment. 2024 Jul 24:175033.
59. Felice F, Moschini R, Cappiello M, Sardelli G, Mosca R, Piazza L, Balestri F. Is Micronutrient Supplementation Helpful in Supporting the Immune System during Prolonged, High-Intensity Physical Training?. Nutrients. 2024 Sep 5;16(17):3008.
60. Huang Y, Guo X, Wu Y, Chen X, Feng L, Xie N, Shen G. Nanotechnology's frontier in combatting infectious and inflammatory diseases: prevention and treatment. Signal Transduction and Targeted Therapy. 2024 Feb 21;9(1):34.
61. UHBlog. 8 Healthy Foods That Can Be Risky in Excess [Internet]. University Hospitals. 2024 [cited 2024 Dec 9]. Available from: https://www.uhhospitals.org/blog/articles/2024/06/8-healthy-foods-that-are-risky-in-excess
62. UF Health [Internet]. [cited 2024 Dec 9]. Selenium in diet. Available from: https://ufhealth.org/conditions-and-treatments/selenium-in-diet
63. Flowers-Kelvin E. Buzzrx. 2024 [cited 2024 Dec 9]. Top 9 Selenium Benefits to Improve Health & Well-Being. Available from: https://www.buzzrx.com/blog/selenium-benefits

 doi:10.20944/preprints202502.2251.v1

64. Traven L, Marinac-Pupavac S, Žurga P, Linšak Ž, Žeželj SP, Glad M, Linšak DT, Cenov A. Arsenic (As), copper (Cu), zinc (Zn) and selenium (Se) in northwest Croatian seafood: A health risks assessment. Toxicology Reports. 2023 Dec 1;11:413-9.
65. Fang C, Fu W, Liu N, Zhao H, Zhao C, Yu K, Liu C, Yin Z, Xu L, Xia N, Wang W. Investigating the virulence of coxsackievirus B6 strains and antiviral treatments in a neonatal murine model. Antiviral Research. 2024 Jan 1;221:105781.
66. Luo D, Tang X, Wang Y, Ying S, He Y, Lin H, Khoso PA, Li S. Selenium deficiency exacerbated Bisphenol A-induced intestinal toxicity in chickens: Apoptosis and cell cycle arrest mediated by ROS/P53. Science of The Total Environment. 2024 Feb 25;913:169730.
67. Xiang R, Xiao X, Liu J, Guo Z, He H, Wang X, Wen X, Angelo V, Han J. Protective effects of functional Nano-Selenium supplementation on spleen injury through regulation of p38 MAPK and NF-κB protein expression. International Immunopharmacology. 2024 Mar 30;130:111574.
68. Li Y, Liang J, Jiang C, Cui J, Hong L, Hao Z, Tang Y, Liu Y, Cui X, Teng X. Se alleviated Pb-caused neurotoxicity in chickens: SPS2-GPx1-GSH-IL-2/IL-17-NO pathway, selenoprotein suppression, oxidative stress, and inflammatory injury. Antioxidants. 2024 Mar 18;13(3):370.
69. Nastri BM, Chianese A, Giugliano R, Di Clemente L, Capasso C, Monti A, Doti N, Iovane V, Montagnaro S, Pagnini U, Iovane G. Oreoch-1: A broad-spectrum virus and host-targeting peptide against animal infections. Journal of Peptide Science. 2024 Jul;30(7):e3593.
70. Hamzah AM, Dawood TN. Effect of selenium nanoparticle on lipid profile in local Awassi male lambs. Open Veterinary Journal. 2024 May 31;14(5):1161.
71. Jiao M, Pirozzi CJ, Yu C, Bao X, Hu M, Pan D, Littleton S, Reynolds N, Saban DR, Li F, Li CY. Targeting Catechol-O-Methyltransferase Induces Mitochondrial Dysfunction and Enhances the Efficacy of Radiotherapy in Glioma. Cancer Research. 2024 Nov 4;84(21):3640-56.
72. Zou M, Zheng Z, Xiahou Z, Cao J. Prediction of potential targets and toxicological insights of Astragalus in liver cancer based on network pharmacology: Integrating systems biology, drug interaction networks, and toxicological perspectives. Environmental Toxicology. 2024 Mar 13.
73. Mana N, Theerawatanasirikul S, Semkum P, Lekcharoensuk P. Naturally Derived Terpenoids Targeting the 3Dpol of Foot-and-Mouth Disease Virus: An Integrated In Silico and In Vitro Investigation. Viruses. 2024 Jul 14;16(7):1128.
74. Zhou JF, Zhang MR, Wang Q, Li MZ, Bai JS, Dai Q, Zhang YH, Yan MX, Li XH, Chen J, Liu YY. Two novel compounds inhibit Flavivirus infection in vitro and in vivo by targeting lipid metabolism. Journal of Virology. 2024 Sep 17;98(9):e00635-24.
75. Kamangar F, Chow WH, Abnet CC, Dawsey SM. Environmental causes of esophageal cancer. Gastroenterology Clinics of North America. 2009 Mar 1;38(1):27-57.
76. Cyna W, Wojciechowska A, Szybiak-Skora W, Lacka K. The Impact of Environmental Factors on the Development of Autoimmune Thyroiditis. Biomedicines. 2024 Aug 7;12(8):1788.
77. Ibrahim RE, Elshobaky G, ElHady M, Abdelwarith AA, Younis EM, Rhouma NR, Murad SK, Yassin EM, Khamis T, Ismail SH, Davies SJ. Nelumbo nucifera synthesized selenium nanoparticles modulate the immune-antioxidants, biochemical indices, and pro/anti-inflammatory cytokines pathways in Oreochromis niloticus infected with Aeromonas veronii. Fish & Shellfish Immunology. 2024 Jan 1;144:109287.
78. Lopatina AV, Sviridova AA, Belousova OO, Kuzmina US, Melnikov MV. The role of dopamine receptors in the modulation of mononuclear phagocytes in multiple sclerosis. Zhurnal nevrologii i psikhiatrii imeni SS Korsakova. 2024;124(7. Vyp. 2):79-84.
79. Al-Wakeel AH, Elbahnaswy S, Eldessouki EA, Risha E, Zahran E. Dietary biogenic selenium nanoparticles improve growth and immune-antioxidant indices without inducing inflammatory responses in Nile tilapia. Scientific Reports. 2024 Sep 23;14(1):21990.
80. Jahan I, Islam MA, Harun-Ur-Rashid M, Sultana GN. Cancer prevention at the microscopic level with the potent power of micronutrients. Heliyon. 2024 Nov 15;10(21).

 doi:10.20944/preprints202502.2251.v1

81. Chen B, Yu P, Chan WN, Xie F, Zhang Y, Liang L, Leung KT, Lo KW, Yu J, Tse GM, Kang W. Cellular zinc metabolism and zinc signaling: from biological functions to diseases and therapeutic targets. Signal Transduction and Targeted Therapy. 2024 Jan 3;9(1):6.
82. NCBI [Internet]. [cited 2024 Dec 10]. IL1B interleukin 1 beta [Homo sapiens (human)] - Gene. Available from: https://www.ncbi.nlm.nih.gov/gene/3553
83. Chilala P, Skalickova S, Horky P. Selenium Status of Southern Africa. Nutrients. 2024 Mar 27;16(7):975.
84. Mayo Clinic [Internet]. [cited 2024 Dec 11]. HIV/AIDS - Diagnosis and treatment. Available from: https://www.mayoclinic.org/diseases-conditions/hiv-aids/diagnosis-treatment/drc-20373531
85. Hyde KD, Baldrian P, Chen Y, Thilini Chethana KW, De Hoog S, Doilom M, de Farias AR, Gonçalves MF, Gonkhom D, Gui H, Hilário S. Current trends, limitations and future research in the fungi?. Fungal Diversity. 2024 Mar;125(1):1-71.
86. Bizerea-Moga TO, Pitulice L, Bizerea-Spiridon O, Moga TV. Exploring the Link between Oxidative Stress, Selenium Levels, and Obesity in Youth. International Journal of Molecular Sciences. 2024 Jul 2;25(13).
87. Alshammari MK, Fatima W, Alraya RA, Alzahrani AK, Kamal M, Alshammari RS, Alshammari SA, Alharbi LM, Alsubaie NS, Alosaimi RB, Asdaq SM. Selenium and COVID-19: A spotlight on the clinical trials, inventive compositions, and patent literature. Journal of Infection and Public Health. 2022 Nov 1;15(11):1225-33.
88. Ağagündüz D, Çelik MN, Çıtar Dazıroğlu ME, Capasso R. Emergent drug and nutrition interactions in COVID-19: a comprehensive narrative review. Nutrients. 2021 May 4;13(5):1550.