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Review Article

Biochemistry Section

Role of Selenium in the Body: A Narrative Review

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ABSTRACT

The maintenance of required levels of essential micronutrients and macronutrients is necessary for the smooth and proper functioning of the body. Any increase or decrease in the levels of these required micronutrients will have an adverse effect on the metabolic activities carried out in the body. The intake of micronutrients differs from region to region, and many micronutrients do not function in their natural form. Selenium is one of the most vital micronutrients required by the body. Numerous organs and systems, such as the cardiovascular system and reproductive system, are affected by selenium deficiency, which is characterised by diminished activity. Consuming selenium in physiologically suitable doses is necessary for maintaining reproductive and general health. Selenium levels that are beyond the permissible range have been associated with infertility. Prolonged exposure to selenium in the environment has been shown to pose a significant danger to human health. It is still unknown how different dietary selenium sources are processed in human bodies, as well as the ideal type or quantity of dietary selenium to maintain metabolic homeostasis and enhance reproductive health. Throughout the world, selenium deficiency is a relatively prevalent cause of various diseases. It is possible to take supplements for selenium deficiency; however, increased levels of selenium, which are toxic, are very close to normal levels. Therefore, it is important to rule out the toxicity brought on by elevated selenium levels when determining the normal selenium concentration.

Keywords: Antioxidant, Folliculogenesis, Infertility, Keshan disease, Selenoproteins

INTRODUCTION

Selenium is a vital micronutrient with an atomic number 34, and the symbol used for selenium is 'Se'. When selenium was first discovered in 1817, it was believed to be poisonous to humans [1]. Klaus Schwarz made the significant discovery that selenium was an essential element needed by organisms in 1957 [1]. Many diseases can result from selenium deficiency. Just as iodine is a crucial component of thyroxine, an essential hormone for the body's healthy operation, selenium, iron, zinc, copper, and calcium are now thought to be necessary for the thyroid gland to function properly, in addition to iodine [2]. Usually, only a sufficient amount of one of these microelements is needed. Selenium is necessary for maintaining several cellular processes, such as DNA synthesis, which is the most fundamental biological process. Diseases related to selenium deficiency are very common among people worldwide [2]. Not many people are aware of the importance of selenium in the body; hence, this review was conducted to raise awareness about it.

Recommended Dietary Allowance of Selenium

According to the World Health Organisation, selenium intake shouldn't exceed 70 micrograms per day [2]. Selenium intake doses vary for males and females. Men should intake 40-70 micrograms, women 45-55 micrograms, and during pregnancy and lactation, the intake should be 60-70 micrograms. In Poland, selenium is consumed daily in the range of 20 to 59 micrograms. In European countries, selenium is consumed in the range of 20-70 micrograms daily [2]. The recommended daily amount of selenium for children increases with age, from 15 micrograms/day (age 0.5) to 50 micrograms/day (age 14) [3]. Therefore, selenium levels in the body must be balanced since deficiencies can lead to neurological issues, cardiovascular problems, cancer, and immunological deficiencies, while excess levels can have the opposite effect [4]. The following table shows the recommended dietary allowances for selenium in the body [Table/Fig-1].

Recommended dietary allowances for selenium					
S. No.	Age	Male	Female	Pregnancy	Lactation
1	Birth to 6 months	15 micrograms	15 micrograms	-	-
2	Upto 3 years	15 micrograms	15 micrograms	-	-
3	4-8 years	50 micrograms	50 micrograms	-	-
4	9-13 years	50 micrograms	50 micrograms	-	-
5	14-18 years	40-70 micrograms	45-55 micrograms	60-70 micrograms	60-70 micrograms
6	19-50 years and above	40-70 micrograms	45-55 micrograms	60-70 micrograms	60-70 micrograms

[Table/Fig-1]: Recommended dietary allowances for Selenium [2,3].

Natural Sources of Selenium

Various regions of the world have varying amounts of micronutrients. In their natural state, many micronutrients are inactive. Selenium concentration in the soil varies based on rainfall, soil type, texture, and the quantity of organic matter present. The plant's assimilation of selenium is influenced by its physicochemical properties, including redox state, pH, and microbiological activity [5,6]. Geographical differences in the selenium content and bioavailability of species in soil and water, the use of selenium-enriched fertilisers, and self-supplementation with selenium all have a significant impact on the selenium concentration in both plant and animal feeds [5,6]. The body converts micronutrients into various forms for absorption. In their natural state, the three most common organic forms of selenium are selenomethionine, methyl selenocysteine, and glutamyl-methyl selenocysteine [1]. The biological action of selenium is mediated by selenocysteine, which is also readily absorbed [7].

Enhanced foods and supplements commonly incorporate inorganic salts, particularly selenium salts, alongside organic molecules (seleno-amino acids) [2]. Selenium functions biologically as selenocysteine

and selenomethionine [1]. Various factors, such as the soil and growth conditions under which crops are grown, can affect the amount of selenium present in dietary sources. Bread, cereals, eggs, meat, fish, dairy products, fruits, and vegetables are the primary sources of selenium. Protein-rich meals, nuts (especially Brazil nuts with over 6 g/g of the product), and fungi such as mushrooms and yeasts (with selenium levels reaching as high as 3 mg/g) are known to have high selenium content. Fruits and vegetables usually contain small amounts of this micronutrient (generally less than 0.5 g/g of the product), which is associated with their high water content and low protein content. However, some fruits and vegetables like garlic, broccoli, cabbage, cauliflower, and kohlrabi can be good sources of selenium [2,6].

ROLE OF SELENIUM IN BODY

For the body to carry out its functions, every component is required in the proper quantity. Any change in these variables, whether positive or negative, can interfere with the body's ability to operate properly [2]. The human body uses selenium for several intriguing functions, including antioxidant, anti-inflammatory, antimutagenic, anticarcinogenic, antiviral, antibacterial, and antifungal properties [8]. Selenoproteins are believed to play a major role in mediating the antioxidant effects of selenium, utilising their selenocysteine (U) residues to catalyse redox-based processes in the cell, blood, and gut [8,9]. A significant portion of the body's selenium pool, between 28 and 46 percent, is stored in skeletal muscle. Selenium levels in the kidney were found to be higher than those in the liver, spleen, pancreas, heart, brain, lung, bone, and skeletal muscle [10].

Myo-Inositol (MI) is a secondary messenger that triggers the formation of the thyroid hormone-requiring chemical hydrogen peroxide (H_2O_2). When Conduct Disorder (Cd) is administered along with a mixture of MI and selenium, the combination protects mouse thyrocytes against the harmful effects of Cd more effectively than MI alone or selenium alone would [5]. Additional research shows that despite the resistance of Caco-2 cells to selenium deprivation, selenium may exert its anticancer properties by upregulating the expression of tumour suppressor-related genes, tumour defence genes, and humoral defence genes, while downregulating the expression of pro-inflammatory genes [11].

The onset of hypothyroidism may result from any loss of MI. Blood mononuclear cells from healthy individuals were challenged with hydrogen peroxide and MI. In-vitro, selenium therapy showed a protective effect on those cells [11]. Numerous examples indicate that selenium supplementation can affect autoimmune thyroid disease; however, its importance is still up for debate. Several instances of autoimmune thyroiditis have been discovered in selenium-deficient areas due to decreased activity of selenium-dependent glutathione peroxidase. The functions of selenium are described in [Table/Fig-2] [9,11,12].

Role of Selenium in the Thyroid Gland

It is believed that iodine is a key component in the formation of thyroxine, a hormone essential for the body's healthy operation and excreted by the thyroid gland. In addition to iodine, selenium, iron, zinc, copper, and calcium are now believed to be essential for the thyroid gland to function effectively [2]. Most often, just enough of one of these microelements is needed.

Increased or decreased selenium levels do not have a direct effect on the functioning of the thyroid gland. The amount of selenium and the activity of selenium-containing proteins in the thyroid gland are not directly influenced by the levels of selenium or proteins containing selenium in the body [1]. There is a selenium-containing enzyme called type I 59-deiodinase that specifically helps activate naturally produced T4 into physiologically active T3 [1]. In cases where selenium levels are low, transforming growth factor can cause fibrosis and damage to thyroid tissue [1]. It is possible to establish a connection between selenium and body weight. For example, there is a link between selenium deficiency and obesity (measured by Basal Metabolic Index (BMI) and body fat percentage) due to impaired selenoprotein synthesis and metabolism, although the underlying mechanisms are not fully understood [12]. Furthermore, a reduced concentration of natural killer cells (NK cells) was observed in the blood of healthy individuals treated with a selenium-containing substance. The data suggest that selenium has a positive impact on autoimmune thyroid disorders [9]. Additionally, reduced selenium levels were found in the blood of patients with Graves' disease and hypothyroidism during CAT [1].

Role of Selenium in the Reproductive System

The preservation of the body's equilibrium depends on selenium. Due to the increased need for selenium during pregnancy, it is important to consider the benefits of selenium supplementation in pregnant women. Appropriate guidelines may need to be established, similar to those for iodine. The importance of selenium to female fertility is currently poorly understood. The development of a healthy oocyte in female reproduction requires several consecutive processes. Folliculogenesis, which is the process through which immature ovarian follicles present at birth develop into mature follicles in adolescence, is an important phase. In-vitro studies on adult ovaries have revealed that selenium controls the development of granulosa cells and the production of 17-estradiol (E2), one of the primary female sex hormones. Mice do not exhibit any Selenoprotein P (SELENOP) characteristics such as male sterility or neurological abnormalities, despite decreased selenoprotein expression [2]. The glutathione peroxidase family of selenoproteins is particularly important for numerous redox reactions associated with male reproduction. The main function of these enzyme isoforms is to catalyse the reduction of organic hydroperoxides (via glutathione), hydrogen peroxide, and lipid peroxides in order to protect and defend cells from oxidative stress [2].

Role of Selenium in the Immunity of the Body

Consuming selenium has an impact on adaptive immunity, including T and B cell activation and function. One immunological characteristic of selenium levels in-vivo is the favourable impact that higher selenium has on CD4+ T helper cell proliferation and differentiation [8]. According to research from the Hoffmann group, a high Se diet (1.0 mg/kg) led to CD4+ T cells differentiating preferentially toward Th1 immunity and producing a significant amount of IFN-gamma [8,13]. Dietary selenium may affect a range of leucocytic effector processes at the cellular level, including adhesion, migration, phagocytosis, and cytokine secretion [14].

Thyroid gland	Reproductive system	Immunity	Cardiovascular system	Cancer	Other function
Helps in production of T4	Leads to female fertility	Impact on adaptive immunity	Anti-inflammatory effect	Anti-oxidant activity	Anti-bacterial
Helps in improving the BMR	Helps in folliculogenesis	Leukocytic effector processes at the cellular level, including adhesion, migration, phagocytosis, and cytokine secretion	Anti-oxidant properties	Reduces the risk of prostate cancer	Anti-inflammatory
Helps in autoimmune disorders	Helps in production of primary female sex hormones				Antiviral

[Table/Fig-2]: Functions of Selenium [9,11,12].

Role of Selenium in Cardiovascular Health

Selenium levels in the blood, erythrocytes, toenails, serum, and plasma have all been shown to be biomarkers of selenium exposure. However, interpreting these biomarkers is challenging as selenium concentrations depend on various factors, including exposure, the type of selenium consumed, selenium metabolism, and pathophysiological responses to conditions characterised by increased oxidative stress or inflammation [10,14]. Kawasaki Disease (KD) is often observed in individuals with low selenium levels, and selenium supplementation can effectively regulate and prevent KD. The discovery that selenium deficiency was associated with KD, a severe form of cardiomyopathy that can be fatal, provided the first evidence of selenium's involvement in cardiovascular function. Selenium deficiency also plays a role in the pathophysiology of various cardiomyopathies and heart failure, further supporting the claim that selenium is crucial for cardiovascular function. Some potential mechanisms of selenium in KD prevention include its antioxidative properties, protection of membranes from lipid peroxidation, increased oxygen transport and utilisation, protection of myocardium from hypoxic damage, and anti-infection effects [15,16]. In a large European cohort, 70% of individuals with worsening heart failure had low serum selenium values. Low selenium levels in these individuals were associated with increased heart failure, lower quality of life, reduced exercise ability, and a worse prognosis [10,17].

Role of Selenium in Cancer

Selenium, a crucial and unique trace element, plays a role in the prevention of various tumour malignancies [18,19]. There is a possibility that as selenium levels increase above a certain point, it may actually raise the risk of thyroid cancer, resulting in a U-shaped relationship similar to those observed between plasma selenium and cancer mortality, alcohol and diabetes, and folate [18]. The main way in which selenium may have anticarcinogenic effects is through selenoproteins, although the exact pathways are still not fully understood. Abnormal expression patterns of glutathione peroxidases and selenoprotein P in colorectal cancer suggest that the antioxidant properties of selenoenzymes play a role in tumour development and carcinogenesis, particularly by scavenging reactive oxygen species and reducing oxidative damage [19]. The preventive effect of selenium against the toxicity of chemotherapy and radiation is particularly noteworthy [20,21]. Selenium has the ability to selectively reduce the negative side effects of anticancer drugs without compromising their anti-tumour effectiveness [22].

Other Functions of Selenium

Selenium acts on different parts of the body through its various chemical forms and is a key component in various enzymes [1]. One such enzyme is glutathione peroxidase, which contains selenium. It has antioxidative effects, helps protect against lipid peroxidation and oxidative damage, and is involved in DNA synthesis. When there is excessive inflammation in the body, oxidative stress occurs, leading to tissue damage [2,14].

EFFECT OF SELENIUM DEFICIT OR EXCESS IN BODY

The levels of micronutrients and macronutrients vary according to the needs of the body and its internal organs. These microelements can have adverse effects on the body if their levels increase or decrease. Imbalances in these elements can lead to numerous disorders, some of which can be fatal [Table/Fig-3].

Effect of Selenium Deficit in Body

Decline in 5'-DI activity: The symptoms of selenium deficiency affect numerous organs and systems, characterised by reduced activity and compromised structures and functions of selenoproteins. As selenium is a crucial component of the enzyme 5'-DI, a deficiency in selenium leads to a sharp decline in its activity [23].

Selenium deficits	Selenium excess
1. Keshan's disease	1. DNA Damage
2. Viral infection	2. Selenosis
3. Decline in 5'-DI activity	3. Decreased production of hormones
4. Autoimmune thyroiditis	

[Table/Fig-3]: Diseases occurring due to Selenium deficit or excess in the body.

Autoimmune thyroiditis: Selenium deficiency is hypothesised to lengthen and worsen the duration and severity of autoimmune thyroiditis. This may be due to decreased activity of the selenoprotein glutathione peroxidase, leading to increased generation of hydrogen peroxide [2,6].

Viral infections: Selenium deficiency has been linked to an increased risk of various infections [24]. The immune system relies on several selenoproteins, including selenoprotein K, which is essential for immune cell functions such as proliferation, migration, cytokine production, and defence against infections, and selenoprotein S, which helps reduce endoplasmic reticulum stress during macrophage activation [7,8]. Pathogens during viral infections cause oxidative stress through the production of reactive oxygen species and alterations in cellular antioxidant defences, including selenoproteins like Glutathione Peroxidases (GPx) and thioredoxin reductases [11,25].

Keshan disease: Keshan disease is a condition caused by selenium deficiency [26]. It primarily affects children and women, with women of reproductive age and children up to age 10 being the most affected [2]. Keshan disease is characterised by cardiomyopathy, with myocardial fibrous replacement and multifocal necrosis [26]. Prospective studies have been conducted to evaluate the effectiveness of sodium selenite in treating Keshan disease in children in endemic regions, but the results were difficult to interpret due to the different active forms of selenium in the body [26].

Kashin-Beck osteoarthropathy: Selenium deficiency also leads to Kashin-Beck osteoarthropathy in children, causing bone deformities, cartilage lesions, and necrosis due to increased oxidative processes [2,27]. Imbalances in selenium can also contribute to arrhythmia, strokes, sudden infant death syndrome, and the exacerbation of immune and autoimmune diseases such as thyroid disorders [28].

Effect of Selenium Excess in Body

The requirements for micronutrients and macronutrients vary depending on the body and its organs. Selenium levels are typically influenced by factors such as region and food intake. Prolonged exposure to high levels of selenium in the environment has been shown to pose a significant health risk to humans [3,5]. Regardless of race or ethnicity, excessive selenium in humans can lead to selenosis and amyotrophic lateral sclerosis. Certain regions in India, known for having selenium-rich soil, are particularly susceptible to this [3,5].

DNA damage: High levels of selenium can lead to the production of excess free radicals, resulting in DNA damage. Selenium helps reduce oxidative stress, thereby protecting DNA from oxidative damage caused by reactive species [29].

Selenosis: Chronic intake of high doses of selenium can cause a condition called selenosis, which is characterised by liver damage. The amount of selenium intake that can cause selenosis depends on the chemical form of selenium and the duration of intake [30].

Decreased hormone production: It is important to note the negative effects of excessive selenium on the endocrine system, including decreased production of thyroid hormones, growth hormone, and insulin-like growth factor [2]. Proper selenium supplementation in diseases like Grave's disease has shown to delay disease progression and improve the quality of life [31].

CONCLUSION(S)

Selenium plays a crucial role in maintaining the overall health and functioning of the body. It is required for various cellular processes and is essential for fundamental biological processes like DNA synthesis. Further prospective research is needed to enhance our clinical understanding of the role of selenium in the body due to its importance. Additionally, more research is necessary to determine the optimal levels of selenium in the body, allowing for supplementation in cases of deficiency while minimising the risk of toxicity.

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