

Role of Selenium

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Abstract:

Selenium(se_{79}^{34}) was a toxic metalloid but after finding that Selenium was essential for preventing Hepatic necrosis in vitamin deficient rats. Selenium is essential for preventing breast cancer via antioxidant effect and cancer, living organisms, sperm motility, reduce the risk of miscarriage, inflammation and immunity, protecting plants against certain diseases, dietary component, metabolism in plants. Selenium is a co-factor for many enzymes. An elevated selenium intake may be associated with reduced cancer risk. Selenium in mercury intoxication in mice also detected in terms of lipid peroxidation. Selenium deficiency causes diseases in animals and human. In human its deficiency called Keshan disease and in animals called White muscle disease (sheep) and Liver cirrhosis (rat). Selenium level falls during oxidative stress.

Keywords: Antioxidant, Oxidative stress, Lipid peroxidation.

INTRODUCTION:

Selenium (se) discovered in 1817 by Jons Jacob Berzelius who named it after Selene, the greek goddess of moon. Selenium is toxic metalloid with wide range of industrial applications including the production of semiconductors, photocopiers, stainless steel, antidandruff shampoos. In 1957 it became evident that selenium essential trace element that prevented hepatic necrosis in vitamin deficient rats(1). About 35 selenoproteins have been identified, though many of their roles were not yet fully elucidated. The best known enzyme is glutathione peroxidase (GPx). This selenoenzyme along with other enzymes such as catalase and superoxide dismutase prevent oxidative damage to cells by breaking oxygen peroxide and other reactive oxygen species. The fact that GPx is selenoprotein and an antioxidant has led investigators to seeking a role for selenium in wide variety of cellular functions and disorders, including immunity, mutagenesis, carcinogenesis, inhibition of viral expression and heart diseases. Selenium has additional important health effects in relations to immune response and cancer prevention which are possibly not exclusively linked to enzymatic functions(2). The only source of selenium for mammalian food chain is food. The amount of selenium in the soil is not equal; it depends on nature of the soil and it is particular on its pH. There are geographic areas with high content of selenium eg. In china, USA and Canada(3). Selenium deficiency has been recognized over 30 years as a factor which limits production in grazing livestock. Diseases associated with selenium deficiency in New Zealand include nutritional myodegeneration (white muscle disease) of lambs, calves and goats, infertility of ewes and ill-thrift of sheep and cattle. Although white muscle disease is most recognizable manifestation of deficiency, sub-clinical deficiencies are more common. Such deficiencies result in decreased growth rate, milk production lambing percentage(4). Selenium commonly found in animal protein, selenium also found in fish, vegetables, brazil nuts. Animal meat and sea food are the richest source of

selenium available to human beings, though it is also present in fairly good amount in cereals, grains, fruits and dairy products(5).

CHEMISTRY OF SELENIUM:

Se was originally discovered by M.H. Klaproth in 1817 in a copper sulfide mine in Falun, Sweden, but misidentified as Tellurium. Later it was named selenium from greek word, selene for moon by J.J. Berzelius. Selenium is 34^{th} in periodic table (atomic mass = 32.066) and is characterized as trace mineral. Se has a +2 charge. In earth's crust, Se is estimated to be present at $10\mu\text{g}/\text{kg}$, although this may vary considerably(6). The element occurs inorganically as selenite, selenate or selenide and its organic forms are predominately selenomethionine and selenocysteine. Selenium is essential component of antioxidant enzyme glutathione peroxidase which protects cell membranes from radical damage(7). In metallurgy it serves as an alloy for cast iron, copper, lead and steel, where as its pharmaceutical use in shampoos(8).

ROLE OF SELENIUM IN HEALTH AND DISEASE:**1. BREAST CANCER:**

The mean serum selenium values in breast cancer patient is significantly less than non-cancer patients. The usage of oral contraceptive pills, being nulliparous and a low serum selenium level are associated with breast cancer (9). An inverse relationship exists between dietary selenium concentration and the incidence of human breast cancer. McConnell et al said that significantly lower mean serum selenium concentration of breast cancer patients as compared to control (10). Charalabopoulos et al found low serum selenium concentration in breast cancer patients but at the same time observed a high concentration in the neoplastic breast tissue. These alterations may reflect part of defence mechanisms against the carcinogenetic process (11). Lopez-saraz et al observed that alterations in serum concentrations of selenium in women with breast cancer appear to be consequence, rather than a cause of cancer. In accordance with hypothesis, the findings suggested that very low

selenium status could be due to nature of cancer (12).The antioxidant functions of selenium have now been shown to reduce the risk of many cancers including breast cancer. Selenium also changes genes that cause cancer. Selenium is an intriguing essential trace element due to its potential role in influencing cancer incidence. Many studies suggest that selenium play an important role in prevention of breast cancer.

2. INFLAMMATION AND IMMUNITY:

Dietary Selenium & selenoproteins are not only important for initiating or enhancing immunity, but they are involved in immunoregulation, which is crucial for preventing excessive responses that may lead autoimmunity or chronic inflammation. On a cellular level, dietary Se may influence various leukocyte effector functions including adherence, migration, phagocytosis, and cytokine secretion. Many members of the selenoprotein family regulate or regulated by cellular redox tone, which is a crucial modulator of immune cell signaling and function. There are also important links between selenoproteins and calcium (Ca^{2+}) flux, which is regulated by and regulates the oxidative burst required for optimal immune cell activation. New insights have been gained into specific roles for individual selenoproteins in modulating immune receptor-mediated signaling pathways linked to calcium flux and oxidative burst, inducing cytokine production, migration, and other cellular processes. This will describe redox-based mechanisms that affect these cellular processes during inflammation and immunity, and how selenium and selenoproteins are involved in those processes. The impact of Se on immune-related human physiology and pathophysiology is also discussed, with emphasis placed on disorders related to immunity and chronic inflammation. Finally, issues are raised as to how supplementation may be best utilized to enhance or modulate certain types of inflammation and immune responses. It should be noted that health issues that hypertension and cardiovascular diseases have been noted (13,14,15)

3. IMMUNE FUNCTION:

Se deficiency depresses the effectiveness of immune cells generally, with diverse specific effects. Supplementation of Se appears to boost cellular immunity by three mechanisms. First, it regulates the expression of the T-cell high-affinity IL-2 receptor (16) and provides a vehicle for enhanced T-cell responses. Since the T cell is a key component in providing B-cell help for antibody synthesis, this may explain the stimulatory effects of Se on antibody production. In fact, age-related decreases in cellular immunity can be partially reversed by Se supplementation increasing responsiveness to IL-2 (16). Second, it prevents oxidative-stress-induced damage to immune cells. Third, it alters platelet aggregation by decreasing the ratio of thromboxane to leukotriene production. Human diseases also associated with Se deficiency.

4. VIRAL INFECTION:

Selenium deficiency is linked to occurrence, virulence, or disease progression of some viral infections (17). Beck (18) has shown that the host where the deficiency of selenium, harmless viruses can become virulent. The study undergone in China, that the rate of infection is lower where the selenium content is normal when compared to the places where the selenium content is low (19). Selenium is seen to be very important nutrient for HIV-infected individuals. Selenium has been used to inhibit HIV activation *in vitro* (20). Many authors said that progressive decline in plasma selenium in parallel with ongoing loss of CD4 T cells in HIV-1 infection. This fall in selenium status even in first stages of disease when malnutrition or malabsorption cannot be a factor (21). Dietary selenium level will influence the diffusion of HIV-1 in Sub-Saharan Africa (22-24). Such countries as Zaire, Uganda, Tanzania, Kenya and South Africa, these are the places where AIDS is the major cause for mortality, are all known to be deficiency of selenium. Keshan disease and Myxoedematous cretinism caused by joint selenium and deficiency of iodine also in the places of Sub-Saharan Africa (25).

5. ANTIOXIDANT:

The high level production of reactive oxygen species (ROS) can exert oxidative stress in physiological system and if excessive amount of ROS is not regulated properly they may cause damage to cellular lipids, proteins and DNA. This damage is related to various human diseases including heart disease. The presence of ROS can also cause the oxidation of low-density lipoprotein (LDL) and it is associated with atherogenesis in heart diseases (26). The only solution is that high selenium content as antioxidant selenoenzymes and selenoproteins that may reduce the oxidized LDL and also reduce the heart diseases (27). There are many animal studies that indicated the important role of selenium in reducing and preventing the incidence of cancer initiated by the variety of carcinogens (28). The generation of ROS in a limited dose is one of the processes induced by the immune system to kill microbial pathogens and viruses. However, increasing in amount of production of ROS can also cause damage to the host cells that need to be prevented by Se at various stages in the immune system. Keshan disease, an endemic cardiomyopathy in China that develops as a result of Se deficiency, may also be complicated with viral infection, and this has led to investigation of the effects of viruses, such as coxsackievirus, on Se-deficient animals (29, 30).

CAUSES FOR DEFICIENCY OF SELENIUM:

1. DEFICIENCY IN ANIMALS:

The foundation for our knowledge of selenium nutrition lies in animal studies. In the laboratory, rats fed selenium-deficient diets develop liver necrosis if these diets are also deficient in vitamin E and sulfur amino acids (31). This degenerative liver disease is distinct from fatty liver and liver cirrhosis, and in the past resulted in death within 21 to 28 days. In 1969, selenium was unconditionally useful for rats and chickens in

diets containing adequate levels of vitamin E and the sulfur amino acids. The disease associated with selenium deficiency depends on the species; in contrast to rats, which develop primarily liver necrosis during combined selenium and vit E deficiency, the mouse develops a multiple necrotic degeneration of skeletal muscle, heart, kidney, liver, and pancreas. Reproductive failure also occurs in males of both rodent species due to defective sperm production. New mouse knockout models with deleted selenoprotein genes are now expressing critical roles for Se in neural function (32) and in gastrointestinal disease (33). The nature of selenium deficiency in production animals provides examples of selenium deficiency diseases that could be useful in characterizing selenium's full role in human health (31).

2. DEFICIENCY IN HUMAN:

Selenium deficiency in humans, known as Keshan disease, still occurs naturally in China as an endemic cardiomyopathy that is primarily localized in peasant populations in some hilly and mountainous regions in China with low soil selenium (34). This disease was eliminated in the 1970s by an aggressive selenium supplementation program after a large study involving over 46,000 subjects clearly described that selenium supplementation would prevent against the disease. The intake of unsupplemented selenium for women in these affected areas of China was estimated to be 12 μ g Se/d. This disease does not occur in the US, where Se intakes are 5 to 15 times higher, and it is also unknown in New Zealand, another area with low soil selenium, where intakes are approximately 30 μ g Se/d (35). Deficiency of selenium in human can also occur clinically. The first report in 1979 was in a New Zealand patient undergoing total parental nutrition (TPN) (36). The patient lived in a rural area with low-selenium soils in which endemic white muscle disease in sheep was controlled with selenium dosing. Following surgery and TPN, she developed dry flaky skin & bilateral muscular discomfort and muscle pain. Plasma selenium had dropped to 0.11 μ mol Se/L (9 μ g Se/L) versus 0.32 μ mol Se/L (25 μ g Se/L) immediately before the start of TPN. The patient was then infused intravenously with a 100 μ g Se/d. Within the next week, muscle pain disappeared and she returned to full mobility. Similar TPN-induced cases of muscle pain and cardiomyopathy will lead to death which has been reported in the US. These cases are associated with very low plasma and red blood cell selenium and GPX1 activity, with increased plasma marker enzymes indicative of damage of tissues, and often with white nail beds.

CONCLUSION:

Selenium plays major roles in living organisms. More research is required to explore the "ROLE OF SELENIUM". Selenium helps in prevention of diseases in both animals and human through antioxidants. Adequate selenium is essential for immune function can protect immune system from oxidative damage and also prevention of cancer. Selenium is essential for its antioxidant function in critically ill patients.

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