
REVIEW PAPER**SILICON IN MEDICINE AND THERAPY****Anna Boguszevska-Czubara, Kazimierz Pasternak****Chair and Department of Medical Chemistry
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Abstract

Trace elements are a very important factor affecting functions of living organisms. Silicon, the third most abundant trace element in the human body, is present in all healthy tissues of people. It is especially strongly associated with connective tissues, as it has been found to participate in bone development, collagen formation and mineralization of bone matrix. Silicon has also been suggested to be involved in mammalian hormonal control and to protect people from heart diseases.

An average dietary intake of silicon is about 20-30 mg/person/day, with higher intakes for men than women. Silicic acid or orthosilicic acid are the bioavailable forms of silicon, found mainly in food rich in fibre and whole grains, in vegetables, fruit and in drinking water. Various alcoholic beverages such as beer or wine also contain considerable amounts of silicon. Silicon provided with food is digested in the gastrointestinal tract to silicic acid, which is then absorbed. With blood, it is distributed into various tissues and organs, where it can exert its action. The highest amounts of silicon are accumulated in the kidneys, liver, bone, skin, spleen, lungs, while free orthosilicic acid, not bounded to proteins, occurs in blood. The amount of silicon in tissues decreases with age. Depleted levels of silicon have also been observed in some pathological states e.g. atherosclerosis.

The aim of the paper has been to present the role of dietary silicon in living organisms. Silicon is necessary for the growth and bone calcification and as a biological cross-linking agent of connective-tissue-based membrane structures. This element is considered to have beneficial effects on several human disorders, including osteoporosis, ageing of skin, hair and nails or atherosclerosis. It has also been suggested that silicon and silicic acid may decrease the bioavailability of aluminium by blocking the uptake of the latter by the gastrointestinal tract and impeding its reabsorption in the kidneys, thus protecting an organism against the toxic (especially neurotoxic) action of aluminium. Anticancer, antiatherosclerotic and antidiabetic effects of silicon have also been suggested.

Key words: silicon, silicon metabolism, bone, connective tissue, aluminium toxicity.

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KRZEM W MEDYCYNIE I LECZNICTWIE

Abstrakt

Pierwiastki śladowe s¹ bardzo ważnym czynnikiem warunkuj¹cym prawidłowe funkcjonowanie organizmów żywych. Krzem, trzeci pierwiastek śladowy pod względem rozpowszechnienia w organizmie człowieka, jest obecny we wszystkich zdrowych tkankach. Szczególn¹ rolę odgrywa krzem w tworzeniu i funkcjonowaniu tkanki ściennej, ponieważ bierze on udział w rozwoju kości, tworzeniu kolagenu i mineralizacji macierzy kostnej. Krzem uczestniczy również w kontroli hormonalnej u ssaków oraz w ochronie przed chorobami serca u ludzi.

Dzienna dawka krzemu dla dorosłego człowieka powinna wynosić 20-30 mg, przy czym zapotrzebowanie na krzem jest większe u mężczyzn niż u kobiet. Przystawaln¹ form¹ krzemu jest kwas krzemowy lub kwas ortokrzemowy, którego Źródłem w diecie s¹ zboża, warzywa, owoce oraz woda pitna. Krzemiany z pożywienia s¹ w przewodzie pokarmowym hydrolizowane do śatwo przyswajalnego kwasu ortokrzemowego, który wraz z krwi¹ jest rozprowadzany do wszystkich tkanek i organów. Najbogatsze w krzem s¹ nerki, w¹troba, kości, skóra, śledziona oraz p³uca, a we krwi krzem występuje w postaci wolnego kwasu ortokrzemowego, niezwi¹zanego z białkami. Wszystkie tkanki zawieraj¹ dużo krzemu, gdy s¹ ca³kowicie zdrowe, natomiast jego poziom zmniejsza się w nich wraz z wiekiem człowieka i tkanki ulegaj¹ wówczas stopniowej degeneracji. Zaniżony poziom krzemu obserwuje się również w pewnych stanach chorobowych, na przyk³ad w miażdżycy.

Celem pracy by³a prezentacja zależności między krzemem przyswajalnym z pożywienia a wp³ywem, jaki wywiera on na organizmy żywe. Krzem jest niezbędnym w procesie wzrostu oraz wapnienia i mineralizacji kości, jest również czynnikiem ścieuj¹cym struktury tkanki ściennej. Pierwiastek ten wywiera korzystny wp³yw w pewnych schorzeniach, takich jak osteoporoza, starzenie się skóry, w³osów i paznokci, miażdżycy. Krzem ma unikatowe w³aciwości wi¹zania metali ciężkich w nierozpuszczalne kompleksy, ograniczaj¹c ich szkodliwe dzia³anie. Dodatkowo, kwas krzemowy hamuje wch³anianie glinu i jest antidotum na jego toksyczne dzia³anie. Sugeruje się również jego dzia³anie przeciwcukrzycowe, przeciwmiażdżycowe oraz przeciwnowotworowe.

S³owa kluczowe: krzem, metabolizm krzemu, kości, tkanka ścienne, toksyczność glinu.

INTRODUCTION

Trace elements are a very important factor, affecting functions of living organisms. Although silicon is the second most abundant element in biosphere after oxygen, due to its very poor bioavailability to the human organism, its influence on metabolic processes is only fragmentarily known and poorly understood (BIRCHALL et al. 1996).

The daily recommended intake (DRI) has not been determined yet, although a suggested daily dose of silicon should reach 20-30 mg for an adult, which corresponds to 0.28-0.43 mg kg⁻¹ b.w. a day for a man weighing 70 kg. Dietary sources of silicon are grains (rice, barley, oat, wheat) and grain products (breakfast cereals, bread, pasta), root vegetables (carrots, beetroot, radish, onion, potatoes), bean, corn, fruit (especially bananas) as well as dried fruit (raisins) and nuts. Silicon is highly available from drinking water

and its concentration depends upon the geology of water intake surroundings because Si is derived from weathering rocks and soil minerals (JUGDAOHSINGH et al. 2002, SRIPANYAKORN et al. 2005). Beer and wine are also rich sources of dietary silicon, containing quite high amounts of orthosilicic acid, a Si bioavailable form (THIEL et al. 2004, GONZÁLEZ-MUÑOZ et al. 2008). Drinking infusions of silicon containing herbs (like Common Horsetail, Knotweed, Red Hemp-nettle, Lungwort) can supplement dietary deficits of that element as well as to alleviate symptoms of some diseases (ZIELECKA 1996).

Silicates from food are hydrolyzed into readily available orthosilicic acid in the gastrointestinal tract (BAREL et al. 2005). The exact site where silicic acid is absorbed from the gastrointestinal canal has not been established, although it has been suggested that silicon compounds from food in the presence of hydrochloric acid and other gastric acids in the stomach are broken down into orthosilicic acid, which easily diffuses through mucous membranes into the blood circulation system. In the Framingham and Framingham Offspring studies, values of an average daily silicon availability have been determined as 12.1-13.5 mg for men and 9.9-10.2 mg for women (JUGDAOHSINGH et al. 2002, JUGDAOHSINGH et al. 2004). The peak increase in the serum silicon concentration was observed 60-84 minutes after orthosilicic acid consumption (REFFITT et al. 1999) and 100-120 minutes after ingestion of a silicon-rich meal (13.15 mg) (JUGDAOHSINGH et al. 2002). Kidneys play a key role in silicon turnover. Silicon is readily filtered by the renal glomerulus because it does not form any bonds with plasma proteins (SRIPANYAKORN et al. 2005). Hence, about 70-80% of plasma silicon is eliminated by kidneys within 3-8 hours after meal ingestion (POPPELWELL et al. 1998). Thus, urinary Si excretion is a good surrogate marker of silicon absorption (WIDNER et al. 1998, REFFITT et al. 1999). Silicon in the form of inorganic silicate occurs in large quantities in kidneys and is a constant component of urine. Silica also fulfils a role of protective colloid preventing appearance of urinary stones, although silicon excess may lead to formation of renal deposits and calculus (ZIELECKA 1996). Studies on kinetics of silicon absorption and elimination demonstrated that the organs and tissues characterized by the highest concentrations of silicon are connective tissues, bone, skin liver, heart, muscle, kidneys and lungs (POPPELWELL et al. 1998, JUGDAOHSINGH 2007). The amount of silicon in tissues decreases with age, probably because the organ responsible for silicon absorption and turnover in an organism is the thymus, which undergoes atrophy with age.

INFLUENCE OF SILICON ON THE DEVELOPMENT AND FUNCTIONS OF A LIVING ORGANISM

For a long time, silicon has been thought to be an inactive substance, not participating in biochemical processes due to its overall unavailability to living organisms. Only recently it has been recognized as one of the most essential trace elements in human metabolism.

The highest concentrations of silicon have been found in organs consisting of connective tissues such as the aorta, trachea, bones and skin. The content of silicon in human skin is $49.5 \mu\text{g g}^{-1}$ of tissue, in hair $42.0 \mu\text{g g}^{-1}$ of tissue and in nails $26.12 \mu\text{g g}^{-1}$ of tissue. A high content of silicon in the connective tissue is attributed to its presence in protein complexes, which form the structure of the tissue as a cross-linking entity (ZIELECKA 1996). In animal studies, the aorta, trachea and tendons were found 4 or 5-fold richer in silicon than the liver, heart and muscles. In blood, silicon occurs in the form of free orthosilicic acid, not bounded with proteins, reaching a concentration from 50 to $200 \mu\text{g L}^{-1}$, depending on its content in a diet (D'HAESE et al. 1995). The overall silicon content in a man weighing 70 kg is from 140 to 700 mg, which classifies that element as the third most abundant macroelement, after zinc and iron (SRIPANYAKORN et al. 2005). All tissues contain large amounts of silicon when they are perfectly healthy, but its amount decreases with age and then the tissues undergo gradual degradation. Depleted levels of silicon have also been observed in some pathological states like atherosclerosis or neoplastic diseases (BISSÉ et al. 2005).

In vitro studies showed that orthosilicic acid in a physiological concentration stimulates collagen synthesis and, through an increase in prolylhydroxylase activity in human osteoblasts, it stimulates their differentiation (REFFITT et al. 2003, JUGDAOHSINGH et al. 2004). Much silicon has also been found in human osteoblasts, highly metabolically active cells. In the human organism, silicon is mainly accumulated in sites of active bone growth. Numerous studies have confirmed that silicon actively participates in the process of bone calcification and accelerates the rate of bone mineralization. Silicon deficiency causes deformations or delay in bones formation as well as disorders in joint cartilage and connective tissue formation (RICO et al. 2000).

There is evidence that dietary silicon is able to lower the plasma total, VLDL and LDL cholesterol level (WACHTER et al. 1998) and to significantly inhibit the atherosclerotic process induced by a cholesterol rich diet (PELUSO, SCHNEEMAN 1994). According to some authors, silicon exerts antiatherosclerotic action mainly through increasing membrane permeability and the basal substance of arteries. Studies carried out on animals proved that silicon administered in the form of silica prevented occurrence of endoxan or streptozotocin-induced diabetes (OSCHILEWSKI et al. 1986). Antineoplastic properties of silicon, which can be associated with its influence on the connective tis-

sue synthesis, thereby reducing progress and propagation cancer, have been reported. Synthetic silicon compounds, e.g. silitrans derivatives, applied together with cytostatics, improved manifold the effectiveness of the latter (JANCZARSKI, JANCZARSKI 1991). Silicon also plays a role in immune functions influencing lymphocytes proliferation (SEABORN et al. 2002).

Silicon has a unique property of binding heavy metals into insoluble complexes, thereby limiting their possible harmful effects. Additionally, silicic acid inhibits the gastrointestinal absorption of aluminium, a metal of neurodegenerative action, whose role in the pathogenesis of Alzheimer's disease is stated to be significant. Silicon is reported to be an antidote to aluminium toxicity as it reduces Al bioavailability (BELLIA et al. 1996, REFFITT et al. 1999, DOMINGO 2006).

Silicon metabolism is connected with the turnover of numerous macro- and microelements. With calcium, silicon is involved in the processes of bone decalcification as well as calcification. Silicon is calcium-antagonist, therefore it can regulate calcium and magnesium turnover. It acts synergistically with copper, thus depressing the zinc concentration in tissues. It also antagonises harmful effects of aluminium on osteogenesis. Additionally, silicon influences the metabolism of such elements as P, Cl, Na, K, S, Mo, Co (O'CONNOR et al. 2008). This element is required to remove harmful and toxic heavy metals from the brain (BIRCHALL et al. 1996, PERRY, KEELING-TUCKER 1998, BOGUSZEWSKA et al. 2003).

Disturbances in silicon turnover have been reported in patients suffering from different skin problems or tuberculosis and in persons treated with antibiotics and chemotherapeutics for a long time (O'AROWSKI 1996, CALOMME, VANDEN BERGHE 1997).

SILICON AND BONE

In the 1980s, the earliest studies on silicon biochemistry, carried out by Carlisle, suggested strong connection between a proper level of dietary silicon intake and normal growth of animals (chickens and rats) (CARLISLE 1980). Particularly collagenous tissues, like bones, cartilages, skin and hair were markedly abnormal in Si-deprived animals. Bone health subsequently became the main subjects for researchers studying the biological role of silicon, mainly because osteoporosis, characterized by low bone mass, is a growing health problem worldwide and leads to marked disability, increased mortality and raised health care costs (SRIPANYAKORN et al. 2005, JUGDAOHSINGH 2007).

According to recent studies, silicon is co-located with calcium in the osteoid tissue, thus some interactions between these elements were suspected to occur in processes of bone growth and mineralization (PERRY, KEELING-TUCKER 1998). In the earliest stage of calcification, in active calcification

sites in young bones, there is a direct relationship between silicon and calcium when the calcium content of the preosseous tissue is very low. Therefore, it has been suggested that silicon is associated with calcium in the early stage of bone formation. It was demonstrated that dietary silicon increased the rate of mineralization, especially in calcium-deficient rats (KIM et al. 2009). Evidence has been obtained to indicate that when rats are fed low calcium diets, bone composition is affected by silicon deprivation: the deprivation depressed concentrations of calcium, magnesium, and phosphorus in the tibia and skull (CARLISLE 1980). Additionally, silicon was found to promote the union of a bone after a fracture, in contrast to calcium, which can actually slow down the healing process or interfere with it altogether, especially when calcium levels are very high. All these facts can be interpreted as promoting bone mineralization by silicon under the conditions of a low level of calcium in a diet, but on the other hand it may also indicate interactions between calcium and silicon in the gut lumen, which can reduce the gastrointestinal absorption of silicon (SRIPANYAKORN et al. 2005, JUGD-AOHSINGH 2007).

SILICON AND SKIN, HAIR AND NAILS

Many studies on silicon influence on bone and cartilage formation confirmed, that the element's primary effect is thought to be on matrix synthesis rather than mineralization (CALOMME, VANDEN BERGHE 1997). Silicon in form of orthosilicic acid at physiological concentrations was found to stimulate collagen type 1 synthesis in human osteoblast-like cells and skin fibroblasts. Silicon treatment also enhanced osteoblastic differentiation. The suggested mechanism of orthosilicic acid is to modulate activity of prolyl hydroxylase, an enzyme involved in conversion of hydroxylate proline to hydroxyproline in the process of collagen formation, rather than alteration in collagen type 1 gene expression (REFFITT et al. 2003). Silicon was also reported to be necessary in formation of glycosaminoglycans in bone and cartilage due to its structural role in the cross-linking of glycoaminoglycans in connective tissue. As type 1 collagen and its monomer hydroxyproline are major constituents of skin, the improvement in skin parameters, like hydration or microrelief (roughness), after silicon supplementation indicates on potential regeneration or de novo synthesis of collagen fibers. Treatment with silicon also might improve the glycosaminoglycan structure in the dermis and the keratin structure in hair and nails, what was seen through decrease in hair and nails brittleness (BAREL et al. 2005).

SILICON AND ALUMINIUM TOXICITY

Despite the widespread occurrence of aluminium in the environment as well as its presence in trace amounts in almost all plants and animals, for a long time Al has been considered to be indifferent to living organisms. However, aluminium can have deleterious effects on plants, animals as well as on human beings. In the terrestrial environment, that is in plants, it is responsible for the development of a stunted and brittle root system; in animals and human it causes growth disorders and disturbed neurological functioning (Alzheimer type senile dementia, amyotrophic lateral sclerosis, a type of Parkinson's disease) (DOMINGO 2006). Aluminium is even more toxic in the aquatic environment, where it can be fatal to fish. Acute aluminium toxicity can be associated to its ability to bind to biologically important ligands, like phosphate groups in membranes, DNA and ATP. Aluminium is also able to bind to anionic sites on fish gill epithelia, stimulating excessive mucus production, which causes potentially lethal disturbances in respiration as well as ion transport (PERRY, KEELING-TUCKER 1998). The idea that silicon may be involved in a mechanism to protect against aluminium poisoning, inspired by Si-Al interactions observed in inorganic chemistry, has been checked in numerous experiments. The most recent research shows that silicic acid interacts with metal ions that are basic at physiological pH, such as aluminium. Silicon is involved in relieving Al toxicity in many different biological systems as well as in reducing aluminium bioavailability in humans by reducing its gastrointestinal absorption and enhancing its renal excretion (BIRCHALL et al. 1996, REFFITT et al. 1999). Orthosilicic acid from beer was found to increase the urinary output of aluminium, perhaps by interacting with filterable Al in renal tubules, forming hydroxyaluminosilicates and thus preventing re-absorption of aluminium (BELLIA et al. 1996). These findings may benefit transplant patients in clearing the accumulated aluminium as well as other patients, protecting them from harmful effects of aluminium excess.

The role of silicon in human biology is poorly understood, although the above findings and studies may suggest beneficial influence of silicon on the human organism in some diseases, like osteoporosis, atherosclerosis, progress of diabetes, propagation of neoplastic process as well as occurrence of heart diseases (TURNER et al. 2008). Silicon was also found to reduce negative effects of some processes as skin, hair and nails ageing (JUGDAOHSINGH et al. 2002). It is very important for regenerating tissues, activating vital processes of cells and improving the general immunity of organism. Therefore, further studies on silicon biology, biochemistry as well as silicon homeostasis and its interactions with essential mineral elements as well as with other biologically important molecules are necessary.

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