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ORIGINAL PAPER

CAN THE SILICON CONTENT IN HAIR BE AN INDICATOR OF ATHEROSCLEROSIS RISK?*

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Abstract

Silicon is the second most prevalent element in the Earth's crust and the third most abundant trace element in the human body. Silicon compounds counteract the crystallization of minerals in the urinary tract, impede the deposition of lipid plaques in the walls of blood vessels and through their presence prevent the absorption of calcium compounds, which reduce the elasticity of blood vessels and may cause diseases of the circulatory system. The article presents the results of studies on the level of silicon and magnesium in the hair of patients with atherosclerosis (*N*=137, age 60-94) and the control group of healthy people (*N*=242, age 20-80). The measured silicon content by ICP-OES in healthy people decreases with age, especially after 40 years of age, and ranges from 43.3±7.8 to 22.4±8.4 μg g^{-1}. The average level of silicon in patients with atherosclerosis is much lower and ranges from 14.0±6.7 to 7.9±4.9 μg g^{-1}, depending on the age range. However, a wide spread of Si values is observed in every age group, even in the group of healthy military students living for several years in the same conditions and using the same diet. Among the patients, there is a group with Si levels below 10 μg g^{-1}, a value that does not appear in healthy people, even those aged 70-80. Due to the presence of a concentration range of 10-20 μg g^{-1} among all tested samples, the Si content in the hair cannot be unequivocally considered a certain atherosclerosis marker, although particularly low Si content below 10 μg g^{-1} should be a clear signal heralding a disease. In such patients, there is also a significantly reduced level of magnesium (5-15 μg g^{-1}) compared with the norms adopted in Poland (25-35 μg g^{-1}).

Keywords: atherosclerosis, silicon content, emission spectrometry, hair analysis.

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INTRODUCTION

Silicon is the second most prevalent element in the Earth's crust, and its content is about 27% of elemental mass. For nearly 50 years, silicon has been considered as an essential trace element for higher plants and mammals and for the normal metabolism of higher animals (Carlise 1984, Martin 2013). The highest concentration of silicon has been found in organs consisting of connective tissues, such as the aorta, trachea, bones and skin. A high content of silicon in the connective tissues is attributed to its presence in protein complexes, which form the structure of the tissue as a cross-linked entity. Silicon has been suggested to exhibit roles in the structural integrity of nails, hair and skin, overall collagen synthesis, bone mineralization, reduced metal accumulation in Alzheimer's disease and reduction in the risk of atherosclerosis. This element was found to stimulate collagen type I synthesis in human osteoblast-like cells and skin fibroblast, and to enhance osteoblastic differentiation. Silicon was also reported to be necessary in the formation of glycosaminoglycans in bone and cartilage due to its structural role in the cross-linking of glycosaminoglycan in the connective tissue. Reduction of collagen, proteoglycans and glycosaminoglycans as well as the degradation of elastic fibers are key factors affecting skin aging (Ferreira et al. 2018). Silicon may play a protective role in atherosclerosis through its effects on blood vessel-associated glycosaminoglycans and collagen integrity and function via its crosslinking capacity (Carlise 1984).

Silicon compounds may counteract the crystallization of minerals in the urinary tract, impede the deposition of lipid plaques in the walls of blood vessels and through their presence prevent the absorption of calcium compounds, which reduce the elasticity of blood vessels and may cause diseases of the circulatory system. Silicon is very important for regenerating tissues, activating vital processes of cells and improving the general immunity of organism (Martin 2013).

Many studies suggest beneficial influence of silicon on the human organism in some diseases, but the role and mechanism of this element in humans is still poorly understood. The content of Si in a body is determined by diet, individual demand of each organism, social economic conditions, the content of chemical elements in drinking water, geographical location, environmental pollution, and other factors.

The importance of silicon as a protective factor in atherosclerosis has not been entirely elucidated. So far, only a few papers on this subject have been published. Loeper et al. (1978, 1988) studied the role of silicon in human atherosclerosis. Most citations in the literature on the role of this element in atherosclerosis prevention concern these works. Boguszewska et al. (2003) carried research on groups of patients with acute and with stable ischemic heart disease. Silicon concentrations in the blood serum of both groups of patients were significantly lower than in the control group. Patients with

acute myocardial infarction were also characterized by lower concentrations of silicon compared with those who had stable coronary heart disease. The few remaining studies were carried out on animal models (Oner et al. 2006, Jugdaohsingh et al. 2015, Vide et al. 2015).

Our goal was to test whether there is a relationship between the level of silicon in the body, specifically in hair**,** and the occurrence of coronary atherosclerosis. The existing literature data unanimously confirm that the Si content in the body decreases with age. Atherosclerosis mainly affects older people, over 50 years old, hence it is difficult to resolve what causes the reduction in silicon levels - age or illness. It is also important to answer the question whether the reduction of the elasticity of blood vessels due to the lower silicon content is one of the many causes of atherosclerosis or if the relationship is reverse. Previous studies have been carried out on small groups of people. In the current study, a larger group of healthy people was selected to assess "normal silicon levels" at different ages and to compare with Si levels in patients with coronary atherosclerosis confirmed by coronarography examination.

Cardiovascular diseases are the most common cause of deaths and are an important social problem. In 2015, 17.7 million died due to cardiovascular diseases in the world and 4.2 million deaths were observed in Europe (WHO data). Statistics of these deaths depend mainly on age – 7% died up to 65 years, and 37% over 65 years. Testing the level of elements in hair is a fast, non-invasive and an increasingly popular method. Confirmation of an unambiguous relationship between silicon levels and the likelihood of atherosclerosis could facilitate initial diagnosis of the disease.

MATERIALS AND METHODS

A variety of measurements of Si in hair were made. Comparative tests of the same samples were performed in different laboratories by the following methods: induced coupled plasma optical spectroscopy (ICP-OES), atomic absorption spectrometry with graphite furnace (GF-AAS), electron microscopy and inductively coupled plasma mass spectrometry (ICP-MS) also coupled to laser ablation. Ashed hair samples were used for microscopic examination.

The most similar results were obtained by the GF-ASA and ICP-OES. The basic method was ICP, but in doubtful cases (very low or very high Si level), the results obtained with the ASA method were compared. The ICP-MS method with laser ablation is very convenient to use as it does not require sample mineralization, but it is a semi-quantitative method. Similarly, electron microscopy is not as accurate and precise as spectroscopic methods. The following types of apparatus were used for analytical determinations: CP-OES (ICAP 7400), ASA (AVANTA-Σ).

Patients (N=137, aged 40 -80 years) were selected from women and men attending the Cardiology Clinic of Institute of Cardilogy at Bielanski Hospital (Warsaw). All of them were referred to hospital for coronary examination because of typical heart ischemic symptoms, and coronary heart disease was confirmed by coronary examination. Healthy volunteers (N=242, 20-80 aged) were recruited as controls. The youngest age control group were military students of Military University of Technology. They have been living in the same place for several years, have a similar diet, are regularly monitored for health. The other volunteers came from Warsaw. The study was approved by the local ethics committee.

There is no standard pattern of silicon in hair. A silicon standard of $[NH_4]_2SiF_6$ at 1000 mg dm^{-3} (Single-Element ICP-Standard-Solution by ROTI®Star) was used to plot the calibration graph. The standard stock solution was diluted with deionized water to the concentration level of the analyzed samples. A single sample measurement was repeated three times, the result was averaged and the standard deviation $s(\bar{x})$ of the mean was calculated. Confidence interval (L) was determined from the Student's distribution. In the case of values $t \cdot s(\bar{x}) > 0.05\bar{x}$, the measurements were repeated. Before using the Si analytical procedure, the method was validated – the analyte recovery was 99%. The ICP and ASA methods are characterized by very high precision and accuracy.

Samples of hair of 2-3 cm length were obtained from a few places on the head. Hair without perming or dyeing was cut from the back of the head, close to the skin. The weight of a hair sample was about 200-300 mg. The samples were washed using nonionic detergent (Triton X-100) water solution (1:100) in an ultrasonic bath for 5 min, then were rinsed with high purity water, acetone, water and then dried to constant mass. A dry sample of 150 mg hair was digested in a closed polypropylene tube (8 ml) with 4 ml of nitric acid 65% (Merck), 1 ml of 30% hydrogen peroxide (Merck) and heated at 80°C for 30 min in a microwave station. After cooling to room temperature, the sample was diluted to a final volume of 10 ml with Mili Q water and then was analyzed.

RESULTS

The age groups of patients with atherosclerosis, the reference persons and their average Si levels are shown in Table 1.

The results of silicon level measurements and the developed statistical data are presented in Figures 1-4. Statistical analysis was made using the Statistica (One-way analysis of variance ANOVA) program.

Table 1

Age groups and mean Si content of the subjects

Type of group	Age group	Number of persons	Silicon content (μg g^{-1})
Control	20-30	83	43.3±7.8
	31-40	50	38.7±8.7
	41-50	25	27.9±9.2
	51-60	27	31.3±7.6
	61-70	30	20.6±7.3
	71-80	27	22.4±8.4
Atherosclerosis	<50	5	14.7±4,6
	51-60	28	14.0±6.7
	61-70	58	9.9±6.4
	71-80	26	7.9±4.9
	>81	20	8.8±5.8

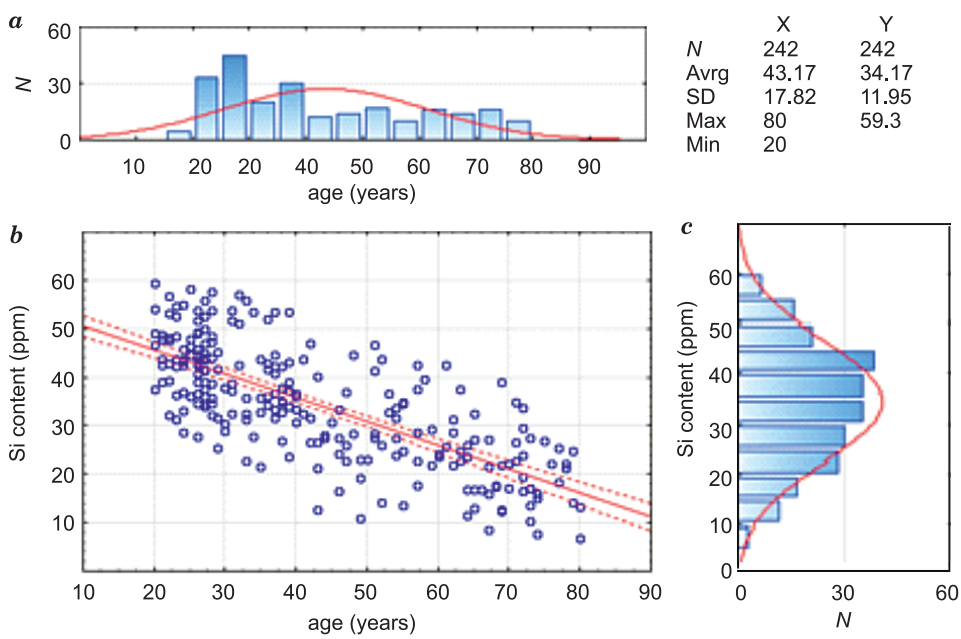

Fig. 1. Silicon content in control group: *a* – diagram of dependence of the number of patients in particular age groups, *b* – diagram of dependence of Si content in hair in particular age groups, *c* – diagram of Si content on the number of patients

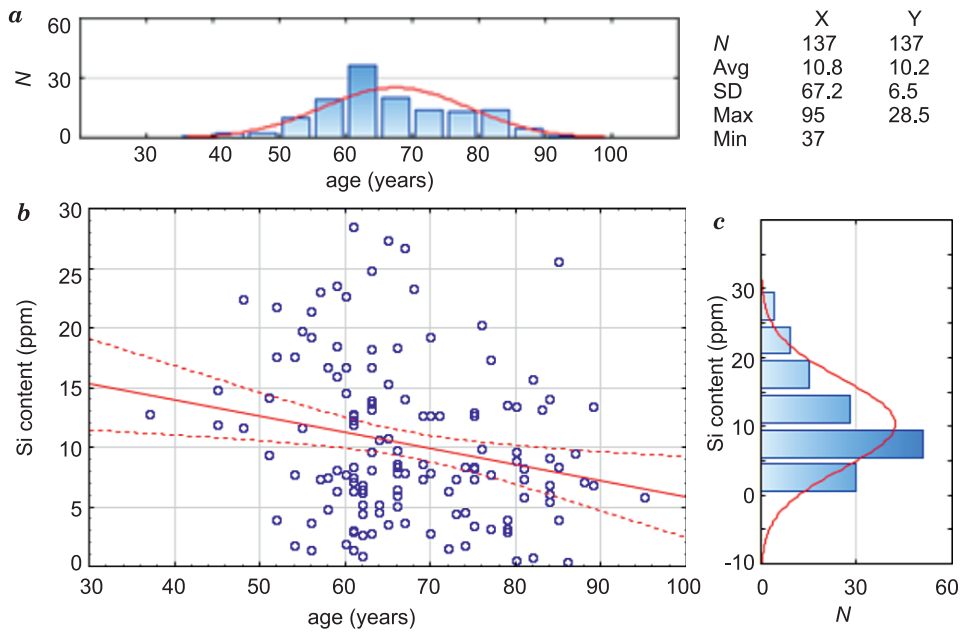

Fig. 2. Silicon content in group of patients with atherosclerosis: *a* – diagram of dependence of the number of patients with atherosclerosis in particular age groups, *b* – diagram of dependence of Si content in hair in particular age groups, *c* – diagram of Si content on the number of patients with atherosclerosis

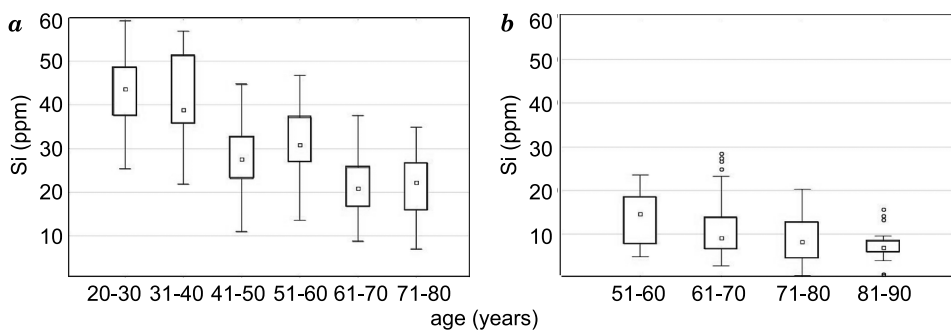

Fig. 3. Diagram of Si content in hair: *a* – control groups, *b* – patients with atherosclerosis

DISCUSSION

The determination of low concentrations of Si in solid biological materials represents one of the current challenges in trace element analysis. This is mainly due to the widespread occurrence of silicon in the environment in general and in the laboratory environment. The Institute of Optoelectronics of the Military University of Technology has made analyses

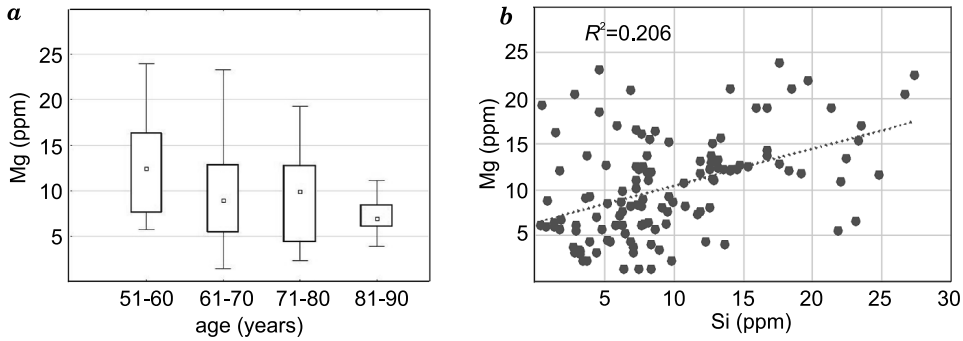

Fig. 4. Diagram of Mg content – *a* and *b* – correlation between Si and Mg of patients with atherosclerosis

of various microelements in materials for 30 years now, but no other element has created so many problems. It is very difficult to establish the normal level of Si in biological fluids and tissues, which is the basis for all comparative investigations and conclusions. Various precautions must be taken to avoid Si contamination, the most important being a) the use of a Class 100 laboratory for sample preparation, and b) applications of strict and elaborate washing procedures for specimen collection tools and laboratory plasticware (Lugowski et al. 2000).

One of the main problems in the analysis of Si in biological matrices is a lack of reference materials. Although Si can be measured in body fluids and tissues, the organic or inorganic form cannot be differentiated by current techniques. Some different analytical techniques, like induced coupled plasma optical spectroscopy (ICP-OES), X-ray fluorescence (XRF) – Haake et al. (2007), electron microscopy, mass spectroscopy, silicon magnetic nuclear resonance spectroscopy (Si-NMR) – Raso, Greene (1997), electrothermal atomic absorption spectrometry (ET-AAS) – Huang, Krivan (2007), or inductively coupled plasma mass spectrometry (ICP-MS) – van Dyck et al. (2000), can be used. Spectroscopic techniques, such as ICP-AES and GF-AAS (AAS with graphite furnace), are currently preferred, and have dominated the determination of Si in biological materials in the last decades. The chemistry of Si in a graphite furnace is quite complicated and not yet fully understood.

Blood, urine and hair are preferred biological material for such analysis. In recent years, the analysis of silicon in human tissues has attracted the attention of numerous researchers due the role of this element in the biochemical and physiological processes. Lately, hair has become an alternative biological specimen to the usual blood, urine and biopsy samples. This method enables monitoring the changes in the trace element status in the body over a long period of time, much longer than in the case of blood samples. The use of hair for tissue mineral analysis is very efficient and relatively accurately reflects the mineral status in a human body. The levels of cer-

tain trace elements in hair are highly correlated with pathological disorders. The affinity of metals for hair is primarily due to the relatively high presence of cysteine in the keratin structure, as well to follicular melanin, which is able to bind cations by ionic interactions (Forte et al. 2005). Hair is second to bone marrow as a metabolic tissue and reflects the level of macro- and microelements in an organism's cells as well as the mineral metabolism rate. Since silicon is an essential trace element, the determination of the "normal" values in tissues is fundamental. For ultra-trace levels of Si in fluids, it is a serious problem. Table 2 presents "normal" levels of Si in whole blood and

Table 2

Normal levels of Si in blood components

Fluid	Authors and year	Method	*N*	Si (μmol dm^{-3})
Serum	Jugdaohsingh et al. (2002)	ICP-OES	8	7.5 ± 3.1
	Teuber et al. (1997)	ICP-AES	55	4.6 ± 2.5
	Leung, Edmond (1997)	ET-AAS	60	1.1 – 7.4
	Dobbie, Smith (1982)	F-AAS	50	21.5 ± 4.5
	Bercowy et al. (1994)	DCP-AES	385	7.1-2421
	Gittelman (1990)	ET-AAS	8	0.60 ± 0.36
Plasma	Bercowy et al. (1994)	DCP-AES	43	14.2-142
	Gittelman et al. (1992)	ET-AAS	14	6.0 ± 1.1
	Roberts, Williams 1990	DCP-AES	20	5.0 ± 0.5

blood constituents published over two decades. The serum level of Si depends on a life stage, age, sex and diet (Lugowski et al. 2000).

In a more recent study including 1325 subjects, Bisse et al. (2005) has established reference values for the serum silicon. In men 18-59 years of age, the median was 9.5 μmol dm^{-3} and decreased to 8.5 μmol dm^{-3} at the age of 60-74. In persons over 74 years of age, the median serum silicone value was 7.7 μmol dm^{-3} for men and 8.0 μmol dm^{-3} for women.

Silicon concentration in hair is higher by two orders than in blood, and the diversity of analytical results is not as high as in the case of blood components. The impact of a determination procedure and impurities in this case is definitely smaller. The results obtained in this study confirm a significant impact of healthy people's age on silicon levels. The reduction of Si level is evident between the age of 20 to 50 years, after which there are smaller decreases in its concentration. It can be assumed that the age-related level of Si is stabilized in the age range of 50-80 years. It is not possible to determine the exact normal Si level for the selected age group.

Loeper et al. (1978, 1988) found that the concentration of silicon in the aortic wall decreases in human atherosclerosis, and this decrease precedes the appearance of lipid deposits. The concentration in silicon decreases

in direct proportion to the severity of atheromatous lesions. It also conserves the integrity of mucopolysaccharides and increases the impermeability of the endothelium, resulting in reduced penetration of lipids. The authors did not confirm any notable or regular decrease in blood lipids through the action of silicon in the serum of rabbits on a high-cholesterol diet. The elastic fibres of rabbits receiving only cholesterol were mostly depleted, thin and fragmented. The results of a more recent study by JUGDAOHSINGH et al. (2015) have shown that dietary silicon has no effect on atherosclerosis development and vascular health in the apoE model of diet-induced atherosclerosis, contrary to the findings of other researchers, including LOEPER et al. (1978, 1988).

On the other hand, NAKASHIMA et al. (1985) noted that the content of glycosaminoglycans in the aorta was inversely correlated with the severity of atherosclerosis. The silicon content in fatty streaks and/or atheroma was significantly higher than in normal human aortic intimal regions, so an increase in the aortic intima is related to the occurrence and/progression of atherosclerosis. Another study indicated that silicon-enriched spirulina (SES) improves early atherosclerosis marker in hamsters on a high-fat diet and the synergy between spirulina and silicon (VIDE et al. 2015).

The statistical characteristics of Si level probability distributions point to a wide dispersion of values. However, a clear effect of age is observed, and an average Si level can be determined for each group (Figure 1). The impact of age on silicon levels described in the literature indicates that the largest changes occur in the 1-40 age range, but we were mainly interested in the group of people at a higher risk of atherosclerotic changes. Figure 5 presents examples of the literature results (LOEPER et al. 1978) of Si levels in the aorta of healthy people and those with atherosclerotic lesions. It may appear that the characteristics obtained are logical when Figures 5*a* and 5*b* are scrutinized separately. Serious doubts arise when we analyze both sets of characteristics together. The reference level of the Si concentration in healthy people, given in Figure 5*b*, was the level in newborns (200 μg 100 mg^{-1} N_2),

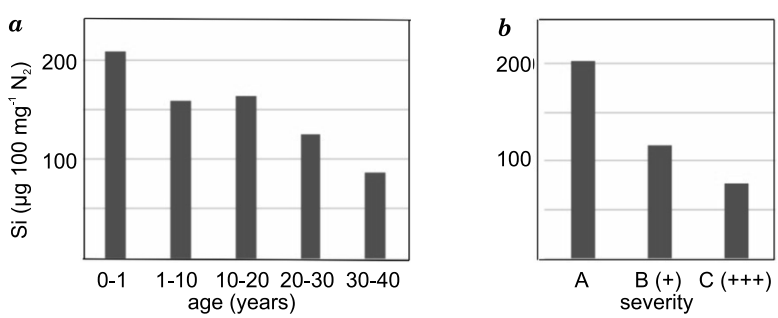

Fig. 5. Distribution of the average silicon content in the human aorta of different ages – *a*, varying severity of atheromatous lesions – *b*: A – normal, B – subendothelial deposit with rarefaction of elastic fibres, C – fatty and calcic deposits including the intima and the media with dissociation of elastic fibres (BOGUSZEWSKA-CZUBARA et al. 2011)

where atherosclerosis does not strike. Atherosclerotic lesions are not smaller. In addition, the authors do not state how many cases this description was based on. Hence, these data are not convincing.

Our research was conducted on a larger group of patients and relevant reference groups of healthy people (Figure 6). Statistical analyses indicate

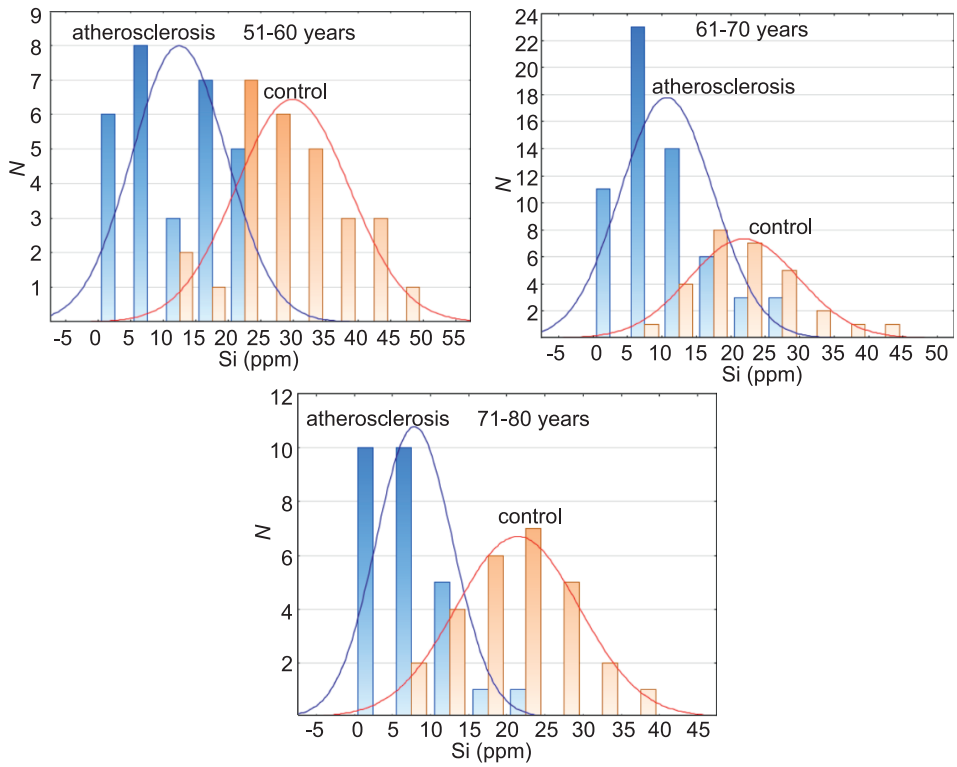

Fig. 6. Statistical comparison of atherosclerotic and control groups, including the age group and the number of subjects in the group, with silicon analysis results

that the level of Si was statistically different in the atherosclerotic groups as compared with the control group, although the difference is not statistically significant (p<0.05), probably due to the small size of the tested group and large statistical deviations of Si values. The χ^2 test results are shown in Table 3.

Table 3

Statistical test results

Age group	p-Value
51-60	0,0411
61-70	0,0328
71-80	0,0308

Our study does not explain whether the low silicon content should be considered as one of the many risk factors for atherosclerosis or if it is a result of chronic atherosclerotic vasculitis.

Although there are differences in the medians of the individual groups, the probability distributions are wide, hence it is difficult to recognize the level of silicon in hair as a characteristic marker of the atherosclerotic disease. For example, the silicon content of 20 μg g^{-1} does not precisely indicate which group a person belongs to. However, it should be noted that among patients with atherosclerotic lesions there is a group with a highly reduced level, of Si below 10 μg g^{-1}. Such a low Si concentration in hair is observed in very few healthy people (Table 4).

Table 4

Percentages of people with silicon content at 10-20 μg g^{-1} and below 10 μg g^{-1}

Type of group	Age group	10- 20 μg g^{-1} (%)	<10 μg g^{-1} (%)
Control	20-30	0	0
	31-40	0	0
	41-50	16	0
	51-60	12	0
	61-70	31	4
	71-80	44	8
Atherosclerosis	<50	80	0
	51-60	32	43
	61-70	35	57
	71-80	27	73
	>81	20	75

Though the mechanism of silicon's anti-atheromatous action remains shadowy, the rise of impermeability of the arterial wall is not the only influencing factor. The Extracellular Matrix (EXM) components in the arterial wall, such as elastin and collagen, determine the stiffness of large elastic arteries (Greenwald 2007). With age and disease, elastic fibers are degraded and fragmented, leading to increased stiffness of the arterial wall. More than 30 elements (Cu, Zn, Mg, Mn, Si, Cr, V and others) have been implicated in the process of atherosclerosis (Anke 1984). Factors such as diet, absorption ability, toxicities and drug-nutrient interaction play a vital role in maintaining a balance of the elements in the body. Copper deficiency as well as its abundance may increase the cholesterol content of the blood serum. It is possible that the formation of crosslinks of elastin in blood vessels is disturbed in Cu deficiency. Zinc deficiency may further aggravate the risk of arterial disease. Chromium deficit may influence the atherosclerotic process via the glucose tolerance factor. Aluminum is considered as a mediator of oxidative stress;

it increases the extra mitochondrial release of free oxygen radicals, resulting in iron-induced peroxidation and protein denaturation of cellular membranes in various organs. Numerous studies have shown that oligomers of silicic acid in the human body effectively prevent gastrointestinal aluminum absorption (JUDGAOHSINGH et al. 2000).

In our research, we additionally tried to establish correlations between silicon and magnesium levels in the group of people with atherosclerosis (Figure 4).

In Poland, the average magnesium content in hair is assumed to be around 25-35 μg g^{-1}. A significant decrease in the magnesium concentration is characteristic for people with cancer (CZERNY et al. 2014). Examining rats receiving different doses of silicon, BOGUSZEWSKA-CZUBARA et al. (2011) showed a significant effect of this element on calcium and magnesium metabolism. The atherosclerotic patient's hair contains less silicon and magnesium than hair of healthy people, but the correlation between these elements is weak (R^2=0.206). Explaining the role of silicon in the body is very important and various aspects of this microelement are still being investigated (PRESCHA et al. 2019).

CONCLUSIONS

The results of tests into the silicon content of hair in healthy people confirmed that there is a distinct decrease in the level of this element with age. The determined "normal" levels of Si in individual groups indicate a wide spread of concentrations, even among people staying in the same place and having the same diet. Si levels in the same age groups of healthy and atherosclerotic patients were compared. Statistically, these are not big differences, but a group with very low Si levels, below 10 μg g^{-1}, was observed among patients with atherosclerosis. Such low silicon levels may be one of the reasons for the increased likelihood of atherosclerosis but recognizing this parameter as a disease marker is risky. To clarify the role of silicon in the formation of atherosclerosis more accurately, one should observe groups of healthy, young people who have lower than average levels of this element. In addition, it is necessary to conduct tests on the silicon content on a much larger number of patients with varying degrees of atherosclerotic disease.

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