The Essentiality of Silicon in Biology

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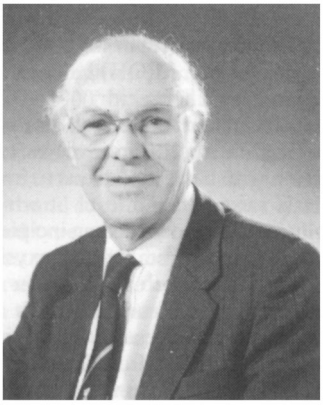
1 Introduction

Consult a modern text on bio-inorganic chemistry[1] and you will find the Periodic Table with the elements essential to life marked – the 'bulk' elements (H,O,N,Na,Ca, *etc.*) and the 15 or so elements (Zn,Cu,Co,Fe, *etc.*) required in trace amounts. Silicon is in this latter group. Silicon is, at 20 atomic percent, the second most abundant element in the earth's crust after oxygen; the third is aluminium at 6 atomic percent. The two are combined in the aluminosilicates of rocks, clays, and soil minerals. There is a massive movement of silicon from its combined state in minerals to its dissolved state as soluble silica – silicic acid, $Si(OH)_4$. At circumneutral pH silicic acid is uncharged and has a solubility of 2mM, above which polycondensation produces oligomeric silicic acids and eventually colloidal particles of hydrated silica, $SiO_2 \cdot xH_2O$. Silicic acid is found in the interstitial water of soils (up to 1mM), in lakes and rivers and in the world's oceans. Rivers, which contain an average of 150 μmol l^{-1} Si, contribute (about 80%) to the flux of dissolved silica to the world ocean which totals 6×10^{12} moles per year.[2] Much of this is utilized by marine organisms such as diatoms, radiolaria, *etc.* in the construction of exoskeletons composed of hydrated, opaline silica. On the death of these organisms, the skeletal structures sink to form a siliceous sediment, some of which is eventually dissolved and recycled. Plants, which can require as much as 600 l of water to form 1 kg dry mass, take in the silicic acid contained in soil water. In some plants this is carried in the transpiration stream and is polymerized as water is lost by evaporation in aerial parts to form opaline silica phytoliths (plant stones) which can stiffen leaves and stalks and reinforce protective spikes and spicules. Such phytoliths return to soil upon plant decay. The average silicon content of terrestrial vegetation is 0.15% – greater than P or Mg – with grasses and cereal crops containing significant amounts. Consequently, herbivores can ingest large amounts of silicon as phytolithic silica: a sheep can ingest 40g Si per day, most of this being phytolithic silica. The total human ingestion has been estimated to be 30 mg Si per day with 60% of this from cereals and 20% from water and drinks[3] and with the latter providing silicon in its most bioavailable form as silicic acid.

Derek Birchall (born 1930) spent most of his career with ICI as a Senior Research Associate. He was responsible for several major inventions including the first commercial production of synthetic inorganic (alumina) fibres. It was work on the toxicity of fibres that introduced him to biology. His time at ICI was interspersed with periods in academe as Visiting Professor at MIT and Industrial Fellow at Wolfson College, Oxford. On retirement from ICI in 1992, Birchall founded the Centre for Inorganic Chemistry and Materials Science at Keele University where he is Professor of Inorganic Chemistry.



He was elected FRS in 1982.

We have a picture, then, of a massive turnover of silicon from geosphere to biosphere with all life exposed to the element.[4] Silicon certainly has a structural function in marine creatures such as diatoms (Figure 1) and in certain plants as hydrated silica. It is considered to be essential in higher animals yet, as is the case for the other essential trace elements, no fundamental biochemical function has been defined and no stable *organic* binding (*via* Si–C or Si–O–C) has been demonstrated for silicon.[5] Silicon appears to enter biology as the neutral species silicic acid and leave it in that form or polymerized as hydrated silica and, in higher animals, with no long-term attachment to the organic chemistry of life. What, then, is the basis of its essentiality?

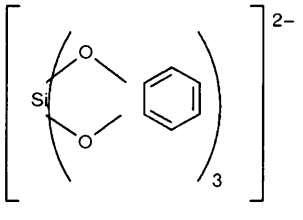
2 Silica Chemistry

The chemistry of silica in solid and dissolved states has been extensively reviewed.[6] It has been remarked (quoted in reference 6) that 'some properties of water and silica are so similar that the transition between hydrated silicic acids and the aqueous matrix is a gradual one.' All forms of solid silica, crystalline and amorphous, dissolve to a limited extent in water at circumneutral pH and at different rates depending on phase, surface area, *etc.* The dissolution and deposition of silica in water may be represented as

$$(SiO_2)_x + 2H_2O \underset{\text{dehydration}}{\overset{\text{hydration}}{\rightleftharpoons}} (SiO_2)_{x-1} + Si(OH)_4$$

At circumneutral pH the equilibrium concentration of monomeric silicic acid is less than 2mM and above this polycondensation produces initially oligomers and eventually colloidal particles of solid, hydrated silica. Such polymerization is responsible for the formation of siliceous skeletons in marine organisms and phytoliths in plant parts. Elegant shapes result because deposition occurs in a delineated space such as within plant cells. In plants, uptake and deposition appears to be a passive process since the silicon accumulated is related to the volume of water transpired and the concentration of the silicon in that water. The construction of the siliceous skeleton of diatoms must be more complex since the concentration of silicic acid in sea water is low and there must be a mechanism for its uptake and concentration to the level at which polycondensation takes place.[7]

In plant and animal physiology, silicic acid can be present in fluids from about 5 to 1000 μ mols per litre and is uncharged, the first proton being lost at above pH 9 and above this pH, the solubility of solid silica rises rapidly as silicate anions are formed. At circumneutral pH, silicic acid in aqueous solution has little chemistry: it interacts with *cis*-diols as in catechol to form complexes such as



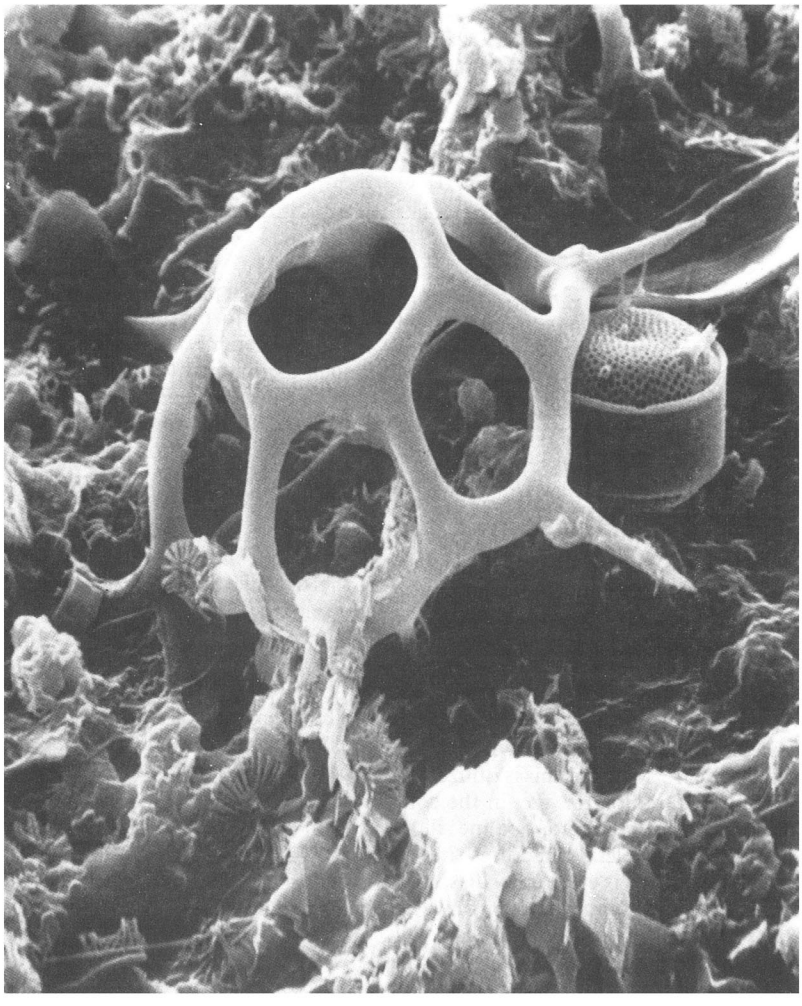


Figure 1 The hydrated silica exoskeletons of diatoms.

but these are stable only above pH 9. There is no evidence of strong interactions between silicic acid and *cis*-diols in sugars for example. That weak (hydrogen bonding) interactions with hydoxyl compounds (*e.g.* gylcols) occur is indicated by the ability of such compounds to reduce the rate of polycondensation of silicic acid at concentrations at which this rapidly occurs normally. It is likely that such weak interactions between silicic acid and solids having hydroxyl groups at their surfaces (*e.g.* cellulose) allow the solid to act as a template for the deposition of silica and dictate bulk morphology and microstructure.[9] However, the presence of Si–O–C bonds has not been demonstrated and is unlikely. Thus, within the biologically relevant range of pH, the *organic* chemistry of silicic acid in aqueous solution is severely restricted. The conclusion of a Ciba Foundation Symposium on 'Silicon Biochemistry' was that no stable organic binding of silicon has been convincingly demonstrated in plant or animal physiology.[5]

Uncharged silicic acid (*i.e.* in solutions below pH 9.8) interacts with metal ions that are basic. Interaction can be detected at a pH about one unit below that at which the metal hydroxide is precipitated. Thus interactions with ferric iron can be detected from pH 2 and above with the hydrolysed species $Fe^{III}(OH)^{2+}$ and $Fe^{III}(OH)_2^+$.

$$\equiv SiOH + Fe(OH)_2^+ \longrightarrow \equiv Si\,O\,Fe^{III}\,O + H^+ + H_2O$$

The colour of ferric iron solutions is discharged by silicic acid and if a 3 molar excess of silicic acid is present, the visible precipitation of the hydroxide is suppressed, an effect used by the water industry. Olation and polymerization occur but the growth of ferric hydroxide particles is restricted to 10—15 nm by the adsorption of silicic acid on particle surfaces. In the case of aluminium, interactions with silicic acids (and its oligomers and colloidal particles) can be detected from pH 4.5 upwards and the formation of species such as $[Al\,O\,Si(OH)_3]^{2+}$ has been conjectured. There are interactions with all basic aluminium species (*i.e.* $[Al(H_2O)_5(OH)]^{2+}$ to $Al(OH)_4^-$), reducing the rate of olation and polymerization. The precipitation of the hydroxide is affected and, as shown in Figure 2, the hydroxide appears to be solubilized. This is again due to retardation of the growth of hydroxide particles as silicic acid adsorbs on hydroxide nuclei.[10] The Si:Al ratio in species formed in solutions containing aluminium and silicic acid rises with silicic acid concentration, reaching 0.5 at a silicic acid concentration of 100 μM (Figure 3). This is the ratio in the mineral imogolite, $(OH)_3Al_2O_3SiOH$, formed when such solutions are heated. This is tubiform in structure and can be considered as a rolled single gibbsite, $Al(OH)_3$, sheet with the inner surface hydroxyls replaced by silicic acid.

Thus the interaction between silicic acid and metals that are basic at circumneutral pH and in dilute solution involves two stages. Initially, there is interaction with basic metal ions to form labile species and then, as pH is raised to the level at which hydroxide nucleation occurs, silicic acid is adsorbed on incipient nuclei, restricting their growth and forming stable hydroxysilicate species. In the case of aluminium, such species can be regarded as fragments of the imogolite structure. Such an adsorption mechanism requires a critical excess concentration of silicic acid over that of the metal ion which, for aluminium is 100 μM Si. We shall see that these interactions with metal ions can influence their bioavailability.

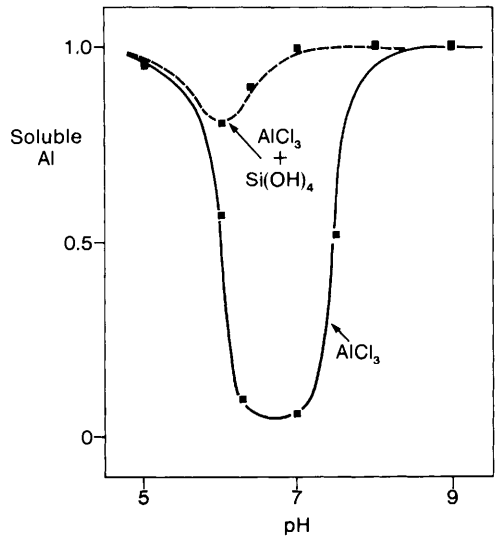


Figure 2 The fraction of aluminium remaining in solution (20h old) after filtration through a 0.2 μm membrane. Solutions contained 0.1 m mol l^{-1} $AlCl_3$ with and without 0.5 m mol l^{-1} $Si(OH)_4$. The growth of hydroxide particles is retarded as hydroxyaluminosilicates are formed.

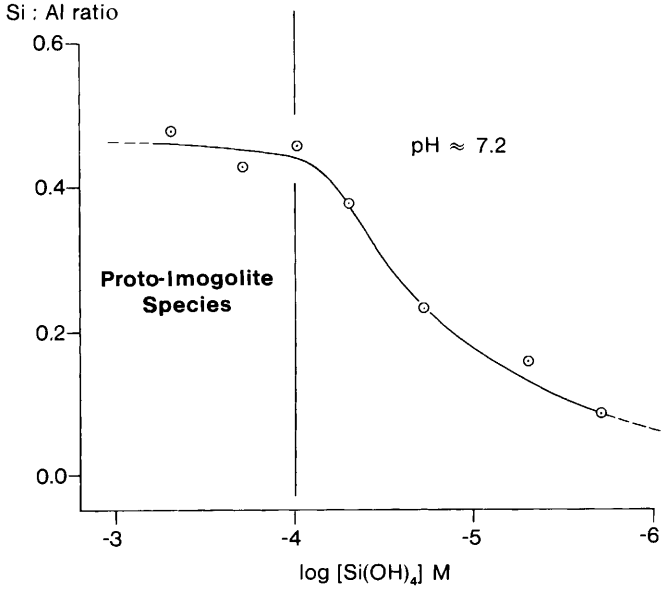


Figure 3 The Si:Al ratio in solid phases formed by the interaction of aluminium species (10 μ mol l^{-1} Al) with silicic acid at pH 7.2.

3 Evidence for the Essentiality of Silicon in Higher Animals

3.1 Early Ideas

Scientific interest in a biological role for silicon dates from the early 1900's when it was considered that silicon was somehow involved in the synthesis and structure of connective tissue (for a review and sources within this section see reference 4). Connective tissue comprises collagen and elastin proteins in a matrix of 'ground substance,' mucopolysaccharides, *etc.* The proportions and type of these components determines the properties of the tissue – the flexibility and toughness of cartilage, the elasticity of arteries and the nature of the organic matrix that is mineralized in the formation of bone. The early association between silicon and such tissue was based on the analysis of connective tissue and its individual components which indicated significant levels of silicon. Whole tissue levels of the order of a few milligrams per 100 g dry weight were commonly reported. Even though the reported levels fell as analytical techniques (usually variations on the molybdate blue method) improved, the concept that connective tissue *contained* silicon led to the idea of silicon compounds as therapy in connective tissue disorders. The first compound used was devised by Ludwig Knorr (U.S. Patent 1,178,731, 1916). This was a product made by the transesterification of tetraethoxysilane and glycerol and it was administered orally to assist in the cicatrization of tubercular lung lesions, *i.e.* their encapsulation in collagen. The use of this material continued until the early 1920's.

This analytical approach persisted. In the 1960's it was reported that the silicon content of the human aorta declined with age from around 200 μg Si per mg N in infants to 80 or so μg Si per mg N at age 40. Furthermore, Si levels in human aortal tissue were reported to fall with increasing sclerotic damage. Again, such analytical studies led to the idea of a therapeutic or preventative role for silicon compounds. In cholesterol-fed rabbits, for example, the oral administration of silicic acid derivatives was claimed to reduce fatty infiltration into the arterial wall and to preserve the integrity of the elastin component. How well-founded were these early ideas associating silicon and connective tissue?

3.2 The Effects of Silicon Deficiency

A powerful way to demonstrate an essential function for an element is to maintain animals on a diet deficient in that element but adequate in all other respects. This requires a very carefully controlled diet and isolation from environmental contamination. Schwarz, using such techniques with rats, had demonstrated the essentiality of selenium, chromium, tin, vanadium, and fluorine.[11] In the late 1960's he turned his attention to silicon and published his findings in 1972.[12] Almost simultaneously, Carlisle published the results of similar studies with chicks.[13] In both studies, silicon deficiency produced defective collagenous connective tissue formation (*i.e.* in articular cartilage) and defects in the growth of bone. In both rats and chicks, growth was very significantly retarded (25—40%) in silicon deficiency and was restored upon the addition of silicon to the diet – up to 500 mg silicate per kg. Figure 4 illustrates the dramatic effect of silicon deficiency on growth and development in the chick.[13] The first mechanistic explanation of such effects was that silicon, bound in the polysaccharidic and protein components of connective tissue, acted as an essential cross-link between the polymer components of connective tissue:[11]

$$R^1\text{–O–}\overset{|}{\underset{|}{Si}}\text{–O–}R^2 \text{ and } R^1\text{–O–}\overset{|}{\underset{|}{Si}}\text{–O–}\overset{|}{\underset{|}{Si}}\text{–O–}R^2$$

Such inter-chain cross-links were thought to stabilize the structure. This hypothesis derived once again from analytical studies in which isolated connective tissue components (*e.g.* collagen, chrondroitin sulfate, *etc.*) were found to contain significant amounts of Si not readily removed (*e.g.* by dialysis, autoclaving *etc.*) and thus regarded as being strongly bound in the macromolecule. For example, hyaluronic acid from human umbilical cord was reported as containing 1892 μg Si per g of which 359 μg per g was considered to be covalently bound. Again, improved analytical techniques including refinement in the molybdate colorimetric method, recognition of the problem of adventitious contamination, and the use of new techniques (plasma emission spectroscopy), led to the conclusion that the earlier findings were erroneous. The Si content of connective tissue and its components was revised to a few μg Si per g dry weight and a structural role for silicon began to be doubted.[14] If not a structural role in higher animals (derived perhaps by extrapolation from its structural role in plants and marine animals) what then?

3.3 A Basic Biochemical Role for Silicon?

Later work by Carlisle (see reference 5) showed silicon to be

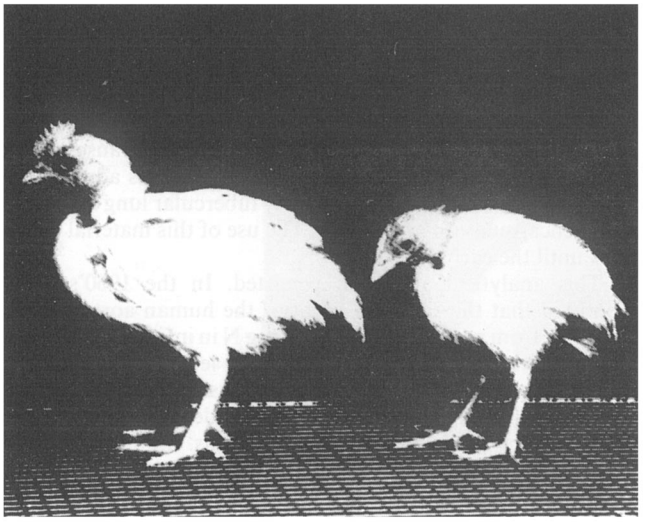


Figure 4 Four week old chicks maintained on a silicon-supplemented diet (left) and silicon-deficient diet (right).
(Reproduced with permission from E. M. Carlisle, *Science*, 1972, **178**, 619.

present in osteoblast cells and to be concentrated at the mineralization front in growing bone, a feature which may be due to osteoblast cells congregating in that region. The analysis of bone indicated a reduction in the proportion of collagenous organic matrix in silicon-deficient bone leading to the conclusion that silicon is involved in collagen biosynthesis. The activity of a key enzyme – prolyl hydroxylase, involved in the hydroxylation of proline in protocollagen – was found to be low in silicon-deficient assay conditions and was raised on silicon addition. A mechanism for such activity could not be suggested, there being no known interaction between silicic acid and the enzyme itself or the essential cofactors – iron, ascorbate, and 2-oxyglutarate. Later studies showed that aluminium present in the system as a contaminant could replace the essential co-factor iron from this enzyme, inhibiting activity. This property of aluminium was suppressed in the presence of silicic acid.[5] This was an early clue that aluminium/silicic acid interactions could be important. Other workers[15] have suggested that silicon increases the activity of adenylate cyclase but, again, no chemistry involving silicic acid has been proposed or found.

Thus a view that silicon is implicated in the synthesis and structure of collagenous connective tissue persists but the idea of its having a structural role as a cross-linking entity has given way to the concept of a role in the synthesis of connective tissue components including the organic matrix of bone.

4 The Effects of Silicon on the Biological Handling of Aluminium

The facts that, in physiology, silicon appears to have no *organic* binding, the chemistry throughout being that of silicic acid, suggests attention should be focused on the *inorganic* chemistry of silicic acid. It is in this area that most recent advances have been made with emphasis on the interactions of silicic acid with aluminium for the following reasons:

- the abundance of aluminium in the environment and its presence as a ubiquitous contaminant
- the well-documented toxicity of aluminium when available to biology
- the strong interactions between aluminium and silicic acid in aqueous systems at circumneutral pH.

For example, the mobilization of aluminium by acidity in soils, rivers, and lakes is responsible for the toxic effect of 'acid rain' on plants and aquatic life.[16] The inadvertent use of aluminium-contaminated water in the dialysis of renal failure patients increased plasma aluminium levels and resulted in a

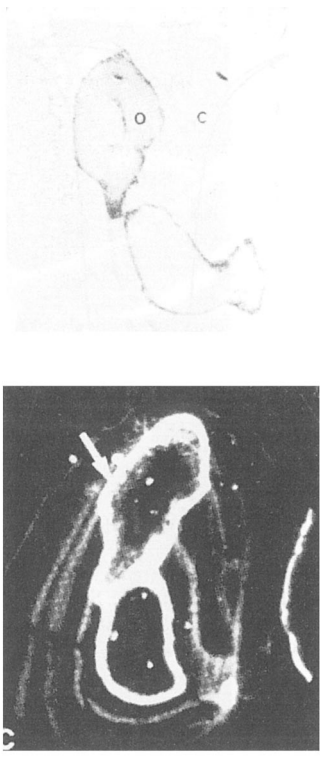


Figure 5 Section through human bone showing aluminium accumulation (arrowed) at the growth front in a patient with dialysis osteomalacia.

serious bone disorder (dialysis osteomalacia) in which aluminium accumulates at the growth front of bone – Figure 5 – together with anaemia and cognitive impairment.

The first test of the idea that silicic acid might mitigate the toxic effects of aluminium was to expose young salmon to acid (*ca.* pH 5) water containing a toxic level (*ca.* 7μ mol l^{-1}) of aluminium with and without silicic acid.[17] In the aluminium-only experiment, all exposed fish died within 48 hours as a result of extensive damage to gill structure and function. In contrast, in the presence of 100 μ mol l^{-1} silicic acid all fish remained healthy with gill function intact (Figure 6). The systemic accumulation of aluminium in the fish (internal organs, bone, *etc.*) was inhibited by silicic acid, the level being reduced from *ca.*2.5 μmol Al per g dry mass to 0.40 μmol Al per g dry mass which is 10% less than found in fish maintained in 'pure' water. This 'aluminium exclusion' effect has subsequently been demonstrated in rats dosed orally with aluminium citrate which is known to promote significant aluminium absorption in the intestine.[18] The presence of silicic acid in the drinking water reduced the absorption and the aluminium concentration in plasma and in soft tissue and completely inhibited the normally very high aluminium deposition in bone. It is thus established that silicic acid can restrict the uptake of environmental and dietary aluminium by plants[19] and animals by forming hydroxy-aluminosilicates having low bioavailability. Do such effects apply in humans?

5 The Effect of Silicic Acid on Aluminium Homeostasis in Humans

In the 1960s and before recognition of its toxicity, plasma and tissue levels of aluminium were raised in renal dialysis patients as a consequence of using dialysis fluid contaminated with aluminium. Water used in dialysis is today subjected to reverse osmosis but a problem of aluminium toxicity remains. This is because it is common for renal failure patients to be given aluminium hydroxide orally to reduce the intestinal absorption of dietary phosphate which they cannot excrete *via* the kidney.

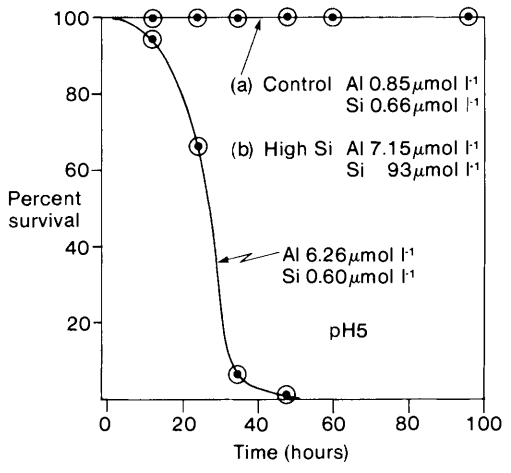


Figure 6 Survival curves for Atlantic salmon fry exposed to control water (low Al and Si) at pH 5 and water containing *ca.* 7 μ mol l^{-1} with high and low silicic acid concentrations.

The accumulation of phosphate in plasma can then lead to the deposition of calcium phosphate in soft tissue. A proportion of the aluminium hydroxide administered is absorbed. There is also an unresolved concern that the slow absorption of dietary aluminium (a few mg per day) may, in vulnerable individuals in the general population, lead to accumulation and contribute to the loss of cognitive function in the aged as in Alzheimer's disease.[2022] Certainly, aluminium absorption can lead to bone disorders in infants and in patients receiving intravenous feeding. Dietary aluminium absorption can be high when the integrity of the intestinal tract is compromised as in infants (due to under development) and the aged (due to degradation). This sort of consideration has caused concerns, for example, about the aluminium content of infant milk based on soya protein, the use of aluminium compounds in medical products, and its concentration in potable water. The human ingestion of aluminium is 5—20 mg/day. The factors influencing aluminium absorption, excretion, and retention may thus not be without consequence.

The fish experiment[17] prompted the suggestion[17,23] that silicic acid would similarly restrict the absorption of aluminium in the human gut and this has been tested. Volunteers were given orange juice containing ^{26}Al with and without 100 μM silicic acid. Using accelerator mass spectrometry, the aluminium levels in plasma were measured 1 and 6 hours after consumption of the drink.[24] The results are shown in Figure 7 which indicates a significant reduction in aluminium absorption in the gastrointestinal tract caused by silicic acid, even in the presence of citrate which is known to enhance absorption.

Silicic acid itself ingested in water and drinks is readily absorbed and rapidly excreted in urine as shown in Figure 8. This illustrates silicon excretion in urine following the consumption by healthy volunteers of water dosed with various levels of silicic acid. In the course of this study it was observed that the peak in silicon excretion in urine was accompanied by a peak in aluminium excretion (Figure 9).[25] The subjects had ingested no aluminium overtly and were not aluminium loaded. Clearly, a background excretion of aluminium is boosted by a surge in silicon excretion. The majority of aluminium in plasma is bound in the iron-binding protein, transferrin, which has a molecular weight too large at 80000 to allow its excretion *via* the kidney. Aluminium in this form in plasma is probably in equilibrium with aluminium bound by citrate (100 μM in plasma) which would be excreted *via* the kidney. Silicic acid is too weak a binder to compete for the aluminium bound in transferrin and its normal concentration in plasma (background 5—20 μM rising to 50 μM following a silicon-rich drink) is low so that it is highly unlikely that hydroxyaluminosilicates form in plasma. A more likely explanation is that silicic acid changes aluminium handling in the kidney. Aluminium (probably as citrate) is passed into

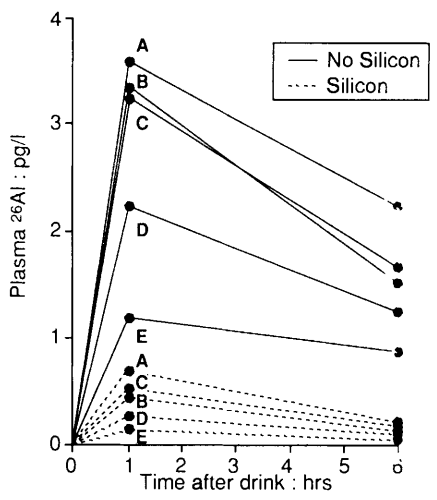


Figure 7 Plasma levels of ^{26}Al in five volunteers A–E 1 and 6 h. after consumption of 75 ng ^{26}Al in orange juice with and without 100 μ mole l^{-1} added silicic acid.)
(Reproduced with permission from J. A. Edwardson *et al.*, *Lancet*, 1993, **342**, 211.)

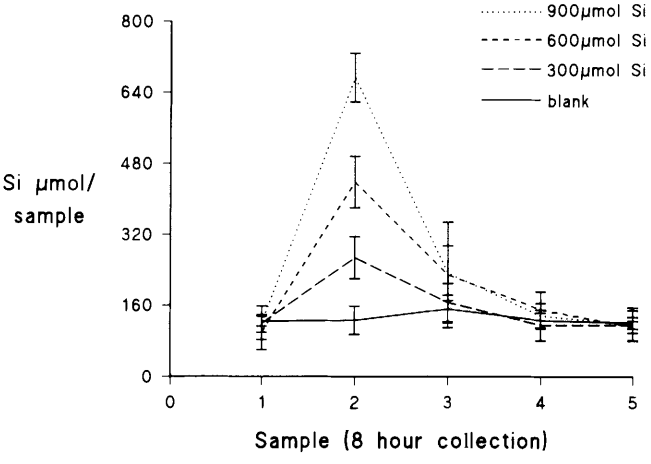


Figure 8 Mean urine excretion of silicon in four healthy volunteers following the consumption of equal volumes of water containing 0, 300, 600, and 900 μM silicic acid.

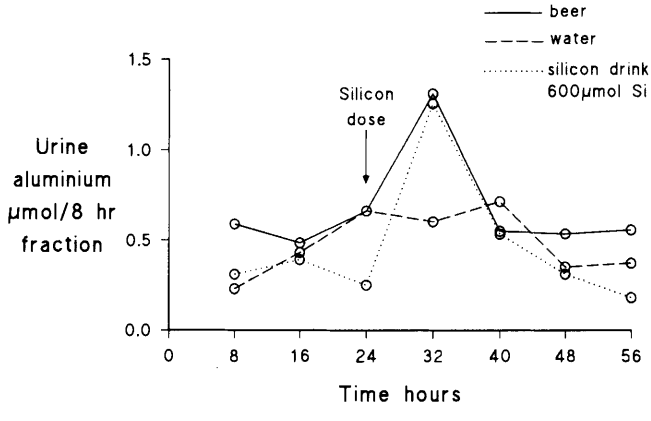


Figure 9 Mean urine excretion of aluminium in healthy volunteers following the consumption of equal volumes of (a) Si and Al-free water containing 4.1% alcohol, (b) beer containing 4.1% alcohol and 600 μM Si, (c) water containing 4.1% alcohol and 600 μM Si (silicon drink). Note that the peak aluminium excretion eight hours after consumption is coincident with maximum silicon excretion – Figure 8.

kidney tubular fluid, some to be excreted in urine and some to be reabsorbed. This balance is altered when the concentration of silicic acid in the tubular fluid is raised to well over 100 μ mol l^{-1} as it clears from plasma and following the consumption of a silicic acid-rich drink (Figure 10). Hydroxyaluminosilicates are then formed in the tubular fluid and are not reabsorbed so that excretion is transiently increased.

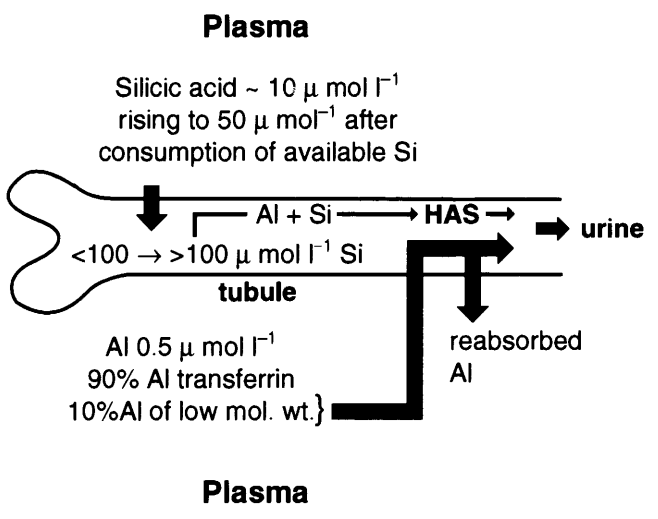


Figure 10 The balance of aluminium excretion/reabsorption in the kidney is altered in favour of excretion when the silicic acid concentration in tubular fluid exceeds 100 μ mol l^{-1} following ingestion and clearance from plasma. Hydroxyaluminosilicates (HAS) are then formed which cannot be reabsorbed and Al excretion is transiently increased.

In inhibiting absorption and enhancing excretion, silicon is clearly involved in aluminium homeostasis in humans and is thus a dietary factor influencing accumulation. The significance of such an effect in healthy people has yet to be discovered. Claims that aluminium levels are elevated in the brains of Alzheimer's patients,[20] influencing neurochemistry[21,22] and recent studies which show that ^{26}Al administered orally in water to rats directly enters the brain[26] all suggest that the 'aluminium exclusion' effect of silicic acid could be important. Silicic acid may also be a factor in the clearance of accumulated aluminium in renal failure patients following kidney transplant.[27]

6 Silicic Acid and other Biologically Significant Elements

The presence of excess silicic acid restricts the growth of ferric hydroxide particles to 15—20 nm and it has been noted that this allows facile reduction and enhanced uptake by chlorotic (iron deficient) plants. Silicic acid appears also to inhibit the excessive uptake of manganese by plants.[4] In the past, such growth-promoting effects have been taken as indicating a positive requirement for silicon whereas the observed effects are due to an indirect effect of silicic acid on the bioavailability of essential and toxic elements. Essential phosphate is strongly adsorbed at the surface of acidic, aluminous soils and is unavailable for uptake by crops. The application of alkaline silicate induces growth. Again, this is due, not to a direct effect of silicon on plant growth, but to the ability of silicate to displace phosphate from its adsorbed state, making it available for uptake. In solution, aluminium is bound to phosphate at pH < 6.6 and to silicic acid at pH > 6.6 and many growth effects produced by adding silicic acid to a system have been attributed to a metabolic requirement when they are in fact due to the mobilization of phosphate.[28]

Historically, silicon has been associated with bone formation and connective tissue (collagen and elastin) synthesis and structure. It is now well established that aluminium affects bone formation and that silicic acid reduces aluminium accumulation in bone. An effect of aluminium on collagen/elastin synthesis is less obvious. However, it has been found that silicic acid influences copper utilization in the rat.[29] The incorporation of 540 mg Si per Kg diet (an amount similar to that found by Schwartz to correct Si deficiency) enhanced copper status in rats as indicated by increased plasma copper concentration, increased ceruloplasmin activity, and an increased copper content in the tissue of heart, liver, and kidney with increased elastin content in the aorta. The authors concluded that some of the metabolic effects attributed to silicon may be due to a silicon-facilitated increase in copper utilization. This could be due to an effect of silicic acid on the gastrointestinal absorption of copper, its transport (ceruloplasmin), or its availability for binding in lysyl oxidase, the copper-dependent enzyme active in the formation of cross-links between the polypeptide chains of the collagen and elastin proteins of connective tissue. The process of cross-linking involves the binding of lysyl oxidase to the telopeptides of molecular collagen/elastin and the conversion of lysyl and hydroxylysine residues into aldehydes. These aldehydes condense with the formation of intra and intermolecular cross-links and this leads to the formation of fibrils of collagen, to the tensile strength, resistance to proteolysis, *etc.* of connective tissue and to the elasticity of the elastin component of connective tissue such as in arteries. It may, then, be significant that dietary aluminium reduces the gastrointestinal absorption of copper and that silicic acid inhibits the gastrointestinal absorption of aluminium.

Copper deficiency gives rise to a variety of defects in bone formation leading to weakness, spontaneous fracture, osteoporosis and, in severe deficiency, to marked bone deformities – some of the defects observed in silicon deficiency. Such effects of copper deficiency are attributed to defective cross-linking in the collagen of the bone organic matrix. Silicon deficiency produces low copper utilization and high aluminium uptake in bone – the former will affect the formation of the organic matrix and the latter its mineralization. Perhaps we now have the beginnings of a mechanistic explanation of the pathological changes produced by silicon deficiency.

Can silicon deficiency exist outside the laboratory? Little is known of the proportion of silicon in diet that is available for absorption and for interaction in the gastrointestinal tract with dietary metals, both essential and toxic. The most available and reactive form is silicic acid and this is readily absorbed, rapidly cleared from tissue and plasma, and excreted in urine. A critical concentration is required at key sites for silicic acid to influence metal handling in the gastrointestinal tract and in the kidney. Given a high clearance rate it may then be that a regular dietary intake is required for the effective control of the homeostasis of some metal components of diet. This remains to be established.

7 Conclusions

The long research on the biological role of silicon, in which the element has been associated with bone and connective tissue formation, may at last be reaching an understanding of mechanism. Because of its ubiquity in the aquatic environment, silicon 'washes through' biology as soluble silica or silicic acid. In some organisms it is concentrated and polymerized to hydrated silica having a structural function. In other organisms it passes through and engages in no organic chemistry. However, it is now clear that it interacts with metals (essential and toxic) influencing their biological availability, uptake, utilization, distribution, and rejection. In spite of its abundance, biology largely excludes aluminium yet requires iron which is less abundant and less soluble. It is perhaps significant that silicic acid increases the availability of iron and reduces that of aluminium. It appears to increase copper utilization in higher animals. The subtle interactions of silicic acid with metals may well have played a vital role in the way biology evolved from its inorganic origins, selecting metals for interaction with the organic chemistry of life and rejecting others. The interaction of silicic acid with metal ions will be an important future topic in bio-inorganic chemistry.

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