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THE CHEMISTRY OF SILICA AND ITS POTENTIAL HEALTH BENEFITS

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Abstract: There is considerable interest in the effects of silica on human health in contrast to prior research which focused solely on the toxic effects of inhaled crystalline silica. However, multiple forms of silica exist in nature and silicon, a component, is the second most prevalent element after oxygen. Silica has widespread industrial applications including use as a food additive, i.e., anti-caking agent, as a means to clarify beverages, control viscosity, as an anti-foaming agent, dough modifier, and as an excipient in drugs and vitamins. Chemically, silica is an oxide of silicon, viz., silicon dioxide, and is generally colorless to white and insoluble in water. When associated with metals or minerals the family of silicates is formed. There are several water soluble forms of silica referred collectively to as silicic acid (ortho, meta, di, and tri-silicates), which are present in surface and well water in the range of 1 - 100 mg/L. Orthosilicic acid is the form predominantly absorbed by humans and is found in numerous tissues including bone, tendons, aorta, liver and kidney. Compelling data suggest that silica is essential for health although no RDI has been established. However, deficiency induces deformities in skull and peripheral bones, poorly formed joints, reduced contents of cartilage, collagen, and disruption of mineral balance in the femur and vertebrae. Very little toxicity data exist regarding aqueous silica consumption due, in part, to the lack of anecdotal reports of toxicity and general presumption of safety. However, a few rodent studies have been conducted, which indicate a No Observed Adverse Effects Level (NOAEL) of 50,000 ppm (mg/L) for dietary silica. In conclusion, many forms of silica exist in nature and compelling data support myriad beneficial effects of silica in water.

Key words: Silica, silicic acid, bone, silicates, silicon.

Introduction

There is renewed growing interest in the beneficial effects of silica on human health. This is in contrast to much of the previous research, which focused on the toxic effects of inhaled crystalline silica and the resultant silicosis that often develops (1). Silicosis is a disease of the lungs caused by continued inhalation of the dust of minerals that contain silica and is characterized by progressive fibrosis and a chronic shortness of breath (2). Probably the most notable example of a detrimental silica compound is asbestos. While there are intrinsic dangers associated with inhalation of crystalline silica, there are multiple forms of silica in nature that are not toxic. Moreover, silica can dissolve in water as silicic acid and it is this chemical form that has received increasing attention as a potentially beneficial component in humans. Collectively, the lack of appreciation of the breadth and diversity of chemical forms of silica has contributed, in part, to the lack of study of potential beneficial effects of aqueous silica. As a result, a clearer understanding of the chemistry of silica, specifically of aqueous ortho-silicic acid, is critical to fostering much needed research on potential health benefits.

Silica is omnipotent in nature making up 26% of the earth's crust by weight and is present in almost all of earth's minerals rocks, sands, and clays. The many forms of silica include quartz, emerald, feldspar, serpentine, mica, talc, clay, asbestos, and glass all of which have different uses. Silica has also been used as an ingredient in steel, in abrasives (silicon carbide), components of transistors (along with boron, gallium, arsenic, etc), solar cells, rectifiers, and other electronic solid-state devices (3). It has also found use as an ingredient of glass when derived from sand-based silica and in the production of computer chips. Silica is also a constituent of filler for paint and rubber ceramics, in lubricants, concrete and bricks, as well as being used for medical devices such as silicone implants. Aside from industrial uses, silica has been used in a nutritional context as a food additive, i.e., anti-caking agent in foods, as a means to clarify beverages and control viscosity, as an anti-foaming agent, dough modifier, and as an excipient in drugs and vitamins. Silica is used biologically by diatoms as a structural component of cell walls. Clearly, silica is omnipresent in the human environment and has a diverse multitude of uses.

Chemically, silica is the oxide of silicon. Silicon is a non-metallic element second only to oxygen in its abundance on earth comprising almost a third of the earth's crust. In its pure form, silicon is unable to exist in its natural state due to its extreme propensity to undergo reactions with ambient oxygen and water. Silica, or silicon dioxide (SiO_2), is found in polymerized combinations with metals and embedded in geologic rock formations. Clearly, silica is widespread and abundant.

Silica also appears in the food chain with concentrations tending to be much higher in plant-based foods, i.e., phytolithic, than animal foods. Beverages, however, are the major contributor to dietary silica, or silicon, and include water, beer (due to barley, hops, etc.), and coffee (4). Silica is prevalent in municipal water supplies but is particularly high in

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bottled spring and artesian waters depending on geological source. In fact, beverages alone contribute to 55% of total dietary intake of silicon as silica. Grains and grain products as part of food contribute around 14% and vegetables contribute 8% (5). It is noteworthy that refinement of grains removes silicon during the process but silica-derived food additives can replace the stripped silicon and increase the content.

The presence of large amounts of silica in geologic formations contributes greatly to the silica content of water. Silica is found in fresh water at concentrations of 1-100 mg/L depending on geographical location. Typical municipal water supplies can provide 4-11 mg/L of aqueous silica as noted in a study of the large cities of France. Levels of around 18-20 mg/L occur in the water of large cities of the United States. Bottled waters also contain modest concentrations of silica ranging from 8 to 36 mg/L as noted for the French brands Badoit, Vichy Celestian, and Volvic (6). Interestingly, water bottled in the Fiji Islands, viz., Fiji water, contains 85 mg/L silica, more than four times the levels found in fresh water and municipal supplies and over twice that of other bottled waters presumably due to the leaching of water-soluble silica from volcanic rock. This provides a clear example of the dependence of the silica content on geologic origin and the wide variation of concentration.

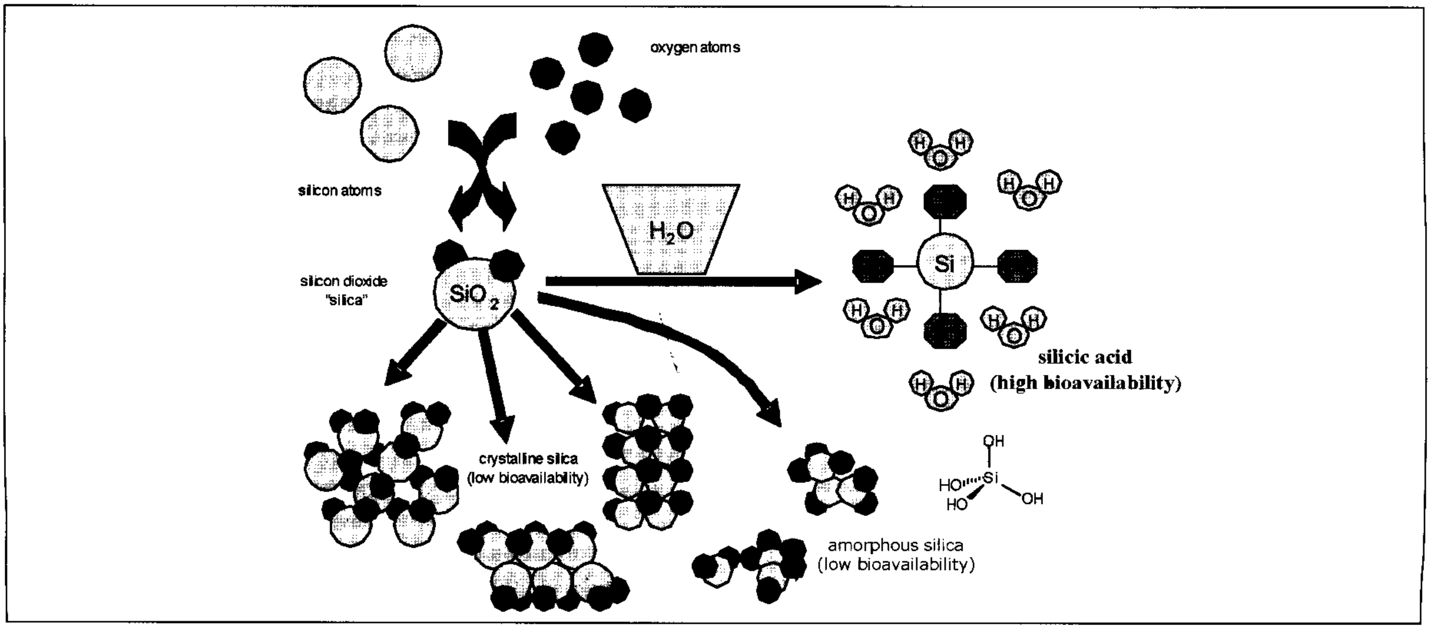
Silica is prevalent in the typical human diet and largely considered safe. However, the lack of clear understanding of the myriad chemical forms of silica has unduly overshadowed the study of the potential protective effects of silica on human health. It is the intent of this review to provide insight into the chemical properties of silica that may render it bioavailable and beneficial to human health.

Chemistry

Silica is a collective term encompassing all reactive (dissolved) and nonreactive (undissolved or colloidal) forms of silicon dioxide or silicates formed from silicon and oxygen in combination with other minerals or metals (Fig. 1). Silicon is a non-metallic element with an atomic weight of 28 and belongs to group IV of the periodic table along with carbon, germanium, tin, and lead. It is tetravalent and the atom is structurally rigid. As expected, the chemistry of silicon is similar to carbon and it can form bonds with many of the same atoms such as silicon-silicon, silicon-oxygen, silicon-nitrogen, and silicon-carbon linkages. However, despite the similarities, substitution of silicon for carbon or vice versa produces a molecule with different properties due, in part, to larger atomic size and greater electronegativity for silicon. Nevertheless, the chemistry of silicon permits a potential role in structural organization of biomolecules such as mucopolysaccharides and collagen. Indeed, observations demonstrate that silica plays a biologically relevant structural role in diatoms as a component of cell walls. It is thus likely that silica can exert biologically beneficial effects in vivo.

Silica occurs in nature in several different forms as crystalline (quartz, critobalite, and tridymite) and amorphous forms. Overall, the chemistry of silica is determined in large part by its strong affinity to oxygen where repeating units of Si-O-Si (siloxane) can occur with remarkable stability. There is some confusion of silica with the term silicone but the two are not the same. Silicone (organosiloxane) refers to man-made siloxane polymers based on a structure of alternating oxygen and silicon atoms. Silicon is not found freely in nature but exists as the oxide and as silicates which involves bonding of

Figure 1
The chemistry of silica



silicon dioxide with various metals.

Although many variations of silica exist, silicic acid is the water-soluble form, $Si(OH)_4$, which is the biologically absorbed and relevant form. Initially, water dissolves silica from sands, rocks and minerals as one of the impurities it collects followed by interaction with the water matrix to form the corresponding silicic acids such as monomeric or ortho-silicic acid, a weak di-protic acid (pK_{a1} 9.6 and pK_{a2} 12.65). There are several water soluble forms of silica classified as ortho (H_4SiO_4), meta (H_2SiO_3), di ($H_2Si_2O_5$), pyro ($H_6Si_2O_7$), and tri-silicates according to the acid origin. Water silicates can liberate orthosilicic acid to a concentration of 1-15 mg/L but concentrations can be as high as 120 mg/L. Beyond this, supersaturation causes dehydration and polymerization to less soluble forms of silica.

Dissolved silica is hydrated to form silicic acid as stated above and associated with anions to counter balance the charge and stabilize the molecule. As a result, shifts in pH can affect the chemical interactions. For example, at pH < 9 silica is present predominantly as silicic acid (SiO_2-$2H_2O$ or H_4SiO_4). However, at low pH silicic acid can polymerize or condense to form uncharged colloids appropriately labeled as colloidal silica. As the pH increases beyond pH = 8, protons dissociate as expected to form bisilicate anions including $H_3SiO_4^-$ and $H_2SiO_4^{-2}$. The increasing ionization and subsequent interaction with water improves solubility of silica and may be the reason that some bottled waters, i.e., Fiji water, can achieve such high silica concentrations. However, more research is needed to confirm this notion. As a caveat, the presence of divalent and polyvalent cations such as calcium, magnesium, etc., can also associate with dissolved, ionized silica to form insoluble salts or silicates. For example, as the pH decreases, pH < 8, silicic acids can form precipitates when the solubility is exceeded. It is noteworthy that reversing the process, i.e., dissolution of precipitate, can be profoundly problematic.

Silica chemistry dictates bioavailability

Bioavailability is the measurement of the rate and extent of an active dietary component that reaches the systemic circulation and is available at the site of action within a tissue or organ target. Bioavailability depends critically on the solubility of compound, which is directly related to the chemical speciation. For example, silicic acid is the form absorbed from gastrointestinal tract and estimates of absorption of silicic acid are 20-75% (7).

Although some of the most abundant materials on earth, silicates do not provide bioavailable dietary silicon. In fact, phytolithic silica (SiO_2-H_2O) occurring in plants is only absorbed around 1-20%. Supplements and pharmaceuticals, crystalline gels and amorphous silica also exhibit very low bioavailability. It would seem possible that solubility could be increased in the GI tract, but this seems to be limited. Cereals provide the greatest amount of silicon in the diet (30%) followed by fruit, beverages (hot, cold, and alcoholic combined), and vegetables. Collectively, these foods provide >75% of the daily silicon intake (4). When silicon is delivered as orthosilic acid as it exists in liquids, it is readily absorbed to >50% of the total ingested amount. Furthermore, silicic acid in foods is also readily absorbed with an approximate absorption of 40%. In one study, humans absorbed only about 1% of a large single dose of an aluminosilicate compound but over 70% was absorbed from a single dose of methylsilanetriol salicylate, a drug developed for the treatment of circulatory ischemia and osteoporosis (8). Proof of absorption of the forms of silicon as silica is verified by daily urinary silicon excretion, as magnesium orthosilicate, of >50% of daily silicon intake. In a bioavailability study, forty-eight hours after ingestion of silicon-32, 36% of the dose was excreted in the urine and elimination appeared to be complete (9).

Although absorption can vary a great deal, the delivery of dietary silica to potential tissue and organ target sites is critical for subsequent benefit although a biochemical function for silicon is unknown. Monomeric silica penetrates all body liquids and tissues at concentrations less than its solubility and is readily excreted primarily in the urine. Findings that as much as 50% of dietary silicon is excreted in urine suggest some forms are well absorbed (10). Moreover, blood silicon levels are significantly higher in patients with kidney failure (11). Concentrations in body fluids approximate plasma levels indicating rapid whole-body dissemination. It is noteworthy that normal human serum has a narrow range of silicon concentration (~50 ug/dl) similar to the concentrations of other dietary trace elements. Silicon is also widely distributed in tissues from plasma. For example, high levels are present in bone, as well as other tissues and organs including nails, tendons, walls of the aorta, RBC, liver, spleen, lung, and kidney. Moderate amounts are found in bone, skin, muscle, and testes. The fingernails contain the highest amount of silicic acid, which is 1500 mg/kg higher than levels in RBC or serum (44 mg/kg and 20 mg/kg, respectively). Various connective tissues including the aorta, trachea, bone tendons, and skin contain most of the silicon in the body (12). Silicon, a surrogate for silica, is found throughout the body at numerous tissue and organ sites.

Silica chemistry determines toxicity

Probably the most noted toxicity associated with silica is silicosis. Silicosis is a disease of the lungs caused by continued inhalation of the dust of minerals that contain silica and characterized by progressive fibrosis and a chronic shortness of breath. The International Agency for Research on Cancer (IARC) classifies silica as a "known human carcinogen" based on inhalation as a route of exposure and dust as the matrix. In an animal study, there was no evidence of cancer when silicon dioxide or amorphous silica, a powder, was given by the oral route to rats and mice for ~2 years. The lack of tumor induction by orally administered silica supports the notion that route of exposure is more critical than form (13). There are limited reports that magnesium trisilicate (6.5 mg elemental silicon) when used as an antacid in large amounts for years may be associated with the development of urolithiasis due to formation, in vivo, of silicon-containing stones (14). However, less than 30 cases have been documented in the last 75 years making it a rare occurrence. Very little toxicity data exists regarding aqueous silica consumption due, in part, to the lack of anecdotal reports of toxicity and general presumption of safety. Moreover, there is no evidence that silicon that occurs naturally in food and water produces adverse effects.

Little acute or chronic data exist on oral toxicity in humans generally due to the lack of any observed toxicity. Limited studies, however, have been conducted in rodents to determine a No Observed Adverse Effects Level (NOAEL). The NOAEL for dietary silica was determined to be 50,000 ppm (mg/L) demonstrating a huge margin of safety. In fact, this is equivalent to 2,500 mg/kg body weight/day for a rodent with the appropriately incorporated safety factors in the experimental design (100-fold). From this, the safe upper level for humans is calculated as 1,750 mg/day for a typical adult male (70 kg). If one considers the highest source of dietary aqueous silica, i.e., Fiji water with 85 mg/L silica, then one would need to consume 20.5 liters, or 86 glasses of water per day, to approach this predetermined upper level of safety. In conclusion, many forms of silica exist in nature. Inhalation of crystalline silica is toxic, but consumption of water soluble silica as orthosilicic acid is not toxic even at very high levels. Moreover, there are compelling data supporting myriad beneficial effects of silica in water, i.e. Fiji bottled water.

Health implications

There a number of studies with compelling results suggesting the essentiality of silicon, delivered as silica, for humans. Indeed, there is continuing debate as to whether there should be an RDI. Silica is omnipresent in US drinking water and is found in surface and well water in the range of 1 - 100 mg/L. However, silica is not listed in the Primary or the Secondary Drinking Water Standards issued by the US EPA. The history of consumption coupled with the lack of anecdotal toxicity of aqueous silica has resulted in relatively little attention to the essentiality of silica-derived silicon.

A functional role for silicon has yet to be identified but clearly it is feasible and likely. Silicon is known to be required by chicks and rats for growth and skeletal development. For example, inducing silicon deficiency produces profound results including deformities in skull and peripheral bones, poorly formed joints, reduced mineral contents of cartilage, collagen, and disruption of mineral balance in the femur and vertebrae. The obvious effect of silicon deficiency on bone supports the notion that it is critical for bone formation as shown in studies with chickens and rats (15-18). Chicks fed silicon-deficient diets also showed structural abnormalities in the skull and long bones such as the femur (12). More in depth studies using rats deprived of silicon showed decreased bone hydroxyproline levels and inhibited alkaline and acid phosphatases (19). Regarding the former, silicon has been shown to contribute to prolylhydrolase activity necessary for normal collagen formation (12). Silica enhances and maintains articular cartilage and connective tissue due to interaction of silicon with glycosaminoglycan formation, a structural building block of these tissues. Silicon is also a constituent of enzyme(s) involved in bone matrix formation suggesting a role in bone calcification. Clearly, silicon is localized in sites of active bone growth supporting a role for dietary silica.

Silicon has also been suggested to exert a protective role in atherosclerosis, in part, due to maintenance of blood vessels (20). For example, increased silica consumption reduces the incidence and severity of atherosclerosis presumably through its effects on blood vessel-associated glycosaminoglycan and collagen integrity and function.

Silica is also thought to be beneficial in Alzheimer's disease because silicon can interact with aluminum and prevent aluminum toxicity often associated with Alzhemier's disease (21). This protective effect has also been noted in humans where dietary silicon protected against aluminum accumulation and presumably neurodegenerative effects (22). Collectively, evidence supports a protective role for silicon in maintaining bone health, cartilage and connective tissue structure, prevention of toxicity to the brain, and maintenance of blood vessel integrity.

Summary and conlusions

Many forms of silica exist with potentially beneficial and detrimental effects. For example, inhaled particulate silica can be toxic and depends heavily on route of exposure and chemical form. Silica can also dissolve in water to form non-toxic bioavailable silicic acids. This form of absorbable silica found in foods and water, and especially bottled waters, is readily absorbed, reaches key tissue and organ target sites of action, and is efficiently excreted. Indeed, there are compelling data to suggest myriad beneficial effects from silica in water on human health. However, the lack of apparent toxicity and the ongoing debate regarding essentiality have obscured the relative importance of different chemical forms and potential contributions of silica.

Further research on silicon is critically needed particularly focusing on the physiological roles of silicon and how this relates to human health, as well as the dependence on chemical speciation. Specifically, ample data exist to support a possible role of silicon in atherosclerosis and hypertension, several bone disorders, Alzheimer's disease, and other conditions know to occur particularly in the elderly. Perhaps the focus of future research should begin with this target population of susceptible individuals.

THE CHEMISTRY OF SILICA AND ITS POTENTIAL HEALTH BENEFITS

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