

Risk Assessment

Silicon

General information

Chemistry

Silicon (Si) is a non-metallic element with an atomic weight of 28. The term 'silica' is used to refer to naturally occurring materials composed principally of silicon dioxide (SiO_2), whereas 'silicone' (organosiloxane) refers to man-made siloxane polymers based on a structure of alternating oxygen and silicon atoms.

Natural occurrence

Silicon is not found freely in nature, but occurs chiefly as the oxide and silicates. Silica (SiO_2) occurs in nature in several different forms: crystalline (quartz, cristobalite and tridymite) and amorphous. When exposed to water, silicates liberate orthosilicic acid to a concentration of 1-15 mg/L.

Occurrence in food, food supplements and medicines

High levels of silicon are found in foods derived from plants, particularly grains such as oats (4250 mg/kg wet weight), barley (2420 mg/kg wet weight) or rice. Levels are lower in foods from animal sources. Beer is also a rich source of silica containing 33-60 mg/kg. Silicon is also found in drinking water as orthosilicic acid.

Amorphous silica is used as a food additive, in particular as an anti-caking agent, but also to clarify beverages, control viscosity and as an anti-foaming agent and dough modifier. It is also used as an anti-caking agent and as an excipient in pharmaceuticals for various drug and vitamin preparations.

UK food supplements contain up to 500 mg silicon.

There are no licensed medicines containing silicon as an active component.

Other sources of exposure

Consumption of 2 L/day drinking water could result in consumption of up to 10 mg silicon. Exposure to high levels of airborne silica occurs in occupations such as quarry workers, miners, foundry workers and sand blasters. Silica deposited in the lungs can be slowly absorbed.

Recommended amounts

Although silicon is thought to be essential, recommendations on adequate nutritional intakes have not been established, either by COMA or other advisory bodies.

Analysis of tissue levels and silicon status

Silicon was initially measured by a colorimetric assay, but high-performance liquid chromatographic/electrothermal atomic absorption (HPLC/ETAAS) and atomic absorption spectroscopy (AAS) methods have been developed more recently.

Methods of assessing silicon status have not been established.

Brief overview of non-nutritional beneficial effects

Silicon has been claimed to reduce the incidence and severity of atherosclerosis.

Function

Silicon is involved in the formation of bone and connective tissues. The precise mechanism is uncertain. However, it has been suggested that silicon could facilitate the formation of glycosaminoglycan and collagen components of the bone matrix through its role as a constituent of the enzyme of prolylhydroxylase. Alternatively, silicon could have a structural role as a component of glycosaminoglycans and glycosamino-protein complexes, occurring as silanolate in mucopolysaccharides and linking different polysaccharides in the same polysaccharide chain, or linking acid mucopolysaccharides to protein.

Deficiency

Silicon deficiency has been produced experimentally in chicks and rats. Such deficiency produces deformities of the skull and peripheral bones, characterised by poorly formed joints, defective endochondrial bone growth and reduced contents of articular cartilage, hexosamine, collagen and water. The concentrations of elements such as calcium, magnesium, zinc, sodium, iron, potassium and manganese may also be decreased in the femur or vertebrae.

Silicon deficiency has not been observed in humans.

Interactions

Silicon has been reported to interact with a number of minerals including copper, zinc and germanium. The interaction between silicon and aluminium has been researched in more detail as a means of inhibiting aluminium toxicity. However the results are conflicting and it is possible that silicon levels are too low for any effect to occur *in vivo*.

Absorption and bioavailability

The bioavailability of silicon depends on the solubility of the compound or speciation concerned. It is thought that silicic acid is the form absorbed from the gastro-intestinal tract. It has been reported that the absorption of silicic acid from the gut is 20-75 %.

Distribution and metabolism

Silicon is widely distributed in the tissues. High levels are present in bone, nails, tendons and the walls of the aorta, with nails containing the highest levels (up to 1500 mg/kg). Lower levels are present in red blood cells or serum (approximately 44 mg/kg for red cells and 20 mg/kg for bound silicic acid in plasma). Silicon is also found in breast milk. Silicon has also been found in the liver, spleen and lung. Animal data suggest that high levels of silicon are found in the kidney, liver and lungs with moderate amounts being found in bone, skin, muscle, testes and spleen. Brain tissue contains negligible amounts of silicon.

No data on silicon metabolism have been identified.

Excretion

Silicon is predominantly and rapidly excreted in the urine, with smaller amounts being eliminated in the faeces.

Toxicity

Human data

Few data are available on the oral toxicity of silicon in humans and no acute or chronic toxicity data have been identified. The occurrence of silica stones has been reported in patients on long term antacid therapy with magnesium trisilicate.

If inhaled at high concentrations over prolonged periods, certain forms of silica can cause silicosis. Silica particles are inhaled into the alveoli of the lung, causing tissue damage that ultimately results in fibrosis, which reduces the efficiency of the lungs and results in shortness of breath. IARC has classified silica (by inhalation) as a Group 1 'known human carcinogen', based on human epidemiological data with support from studies in both animals and biological systems. *In vitro* studies have demonstrated that silicon has an inhibitory effect on superoxide dismutase and thus may potentially increase free radical damage.

It is thought that the carcinogenicity of inhaled silica particles is due to local tissue damage and inflammation with the production of reactive oxygen species, which overwhelm cellular defences and damage DNA. This process is considered not to be relevant to oral exposure to silica or silicon.

Chronic occupational exposure to silica by inhalation can also lead to a distinctive nephropathy manifested clinically by albuminuria and hypertension and characterised pathologically by changes in the glomeruli and proximal tubules. This nephrotoxic reaction (as with the respiratory toxicity described above) is thought not to occur by exposure to silicon in food.

Animal data

The acute oral toxicity of silicon (as silica) is low. No significant toxicity or mortality has been reported in animals given doses of up to 3 g/kg bw/day.

Growth rates were reduced, and the concentrations of certain other minerals in the plasma and tissues were affected in rats fed 500 ppm (equivalent to approximately 50 mg/kg bw for young rats) silicon from 3 different silicate forms in the diet for 8 weeks (either tetraethylorthosilicate (TES), sodium silicate or sodium zeolite (Kayonga-male and Jia, 1999)). Of the forms tested, only sodium silicate is relevant to the assessment of silicon in food. Similar results were observed in turkeys fed 270 ppm dietary silicon from the same three sources for 4 weeks.

Similarly, in rats fed up to 5% syloid (amorphous silicon dioxide) for 24 months, treatment was not associated with any significant dose-related effects on growth rate, survival, haematology or microscopic pathology. Liver weights were reduced from 12-24 months in the females fed 2.5% and 5% syloid respectively, although a clear dose-related trend was not apparent. No dose related pathological changes were observed. No dose related increases in tumours were apparent.

Growth was reduced transiently in mice fed up to 5% (equivalent to 7,500 mg/kg bw/day) syloid in the diet for 21 months. The treatment had no effect on haematology or gross or microscopic pathology. It was stated that an increase in tumours attributed to treatment was found in the haematopoietic organs, particularly malignant lymphoma/leukaemia which occurred in the mid-dose female mice only, but this was not considered significant because a statistical trend test was negative.

No data on reproductive toxicity have been identified.

Carcinogenicity and genotoxicity

Silicon was not carcinogenic in mice or rats at 5% in the diet. Silica was negative in the *Bacillus subtilis rec* assay and was not mutagenic in the Ames test. Sister chromatid exchange (SCE) was not induced in Chinese hamster V79 cells at a range of concentrations. Quartz has been reported to induce dose dependent increases in the number of morphologically transformed Syrian hamster cells. Overall, inorganic silicon compounds do not appear to have significant genotoxic potential.

Mechanism of toxicity

No data have been identified on the mechanism of oral silicon toxicity

Dose response characterisation

No data have been identified.

Vulnerable groups

No vulnerable groups have been identified.

Genetic variations

No genetic variations in the handling of silicon have been identified.

Studies of particular importance in the risk assessment

(For full review see <http://www.food.gov.uk/science/ouradvisors/vitandmin/evmpapers> or the enclosed CD)

Takizawa et al., 1988

Groups of 40 B6C3F1 mice were fed 0, 12,500, 25,000 or 50,000 ppm (5%) syloid (silicon dioxide) in the diet for up to 21 months (equivalent to 1,900 – 7,500 mg/kg bw silica or 900 to 3500 mg silicon). The basal silicon level of the diet was not stated. Interim sacrifices were made at 6 and 12 months, such that up to 20 mice completed the dose period. The growth of mice in the top dose group was significantly reduced at the end of the first 10 weeks of the experiment but no other significant differences were apparent. Food consumption was significantly increased in the males fed 50,000 and 25,000 ppm. No significant dose-related effects on haematology or gross or microscopic pathology, including tumours, were observed. Since the decreased growth rate is likely to be due to nutritional imbalance the top dose (equivalent to 7,500 mg/kg bw/day silicon dioxide, or 3,495 mg silicon/kg bw/day) was considered to be a NOAEL.

Groups of 40 Fischer rats were fed 0, 12,500, 25,000 or 50,000 ppm syloid in the diet for up to 21 months. The silicon content of the basal diet was not stated. No significant dose-related effects on food consumption, growth rate, survival, haematology or microscopic pathology were observed. Mineral levels in the tissues were not measured. Liver weights were reduced (by up to 15%) in the 2.5 and 5% females from 12-24 months; a clear dose related trend was not apparent. No dose related pathological changes were observed. No dose related increases in tumours were apparent but a relatively small number of animals were used in the study. The few effects identified may have resulted from a nutritional imbalance and therefore may not be relevant to humans. The top dose (equivalent to 2,500 mg/kg bw/day silicon dioxide, or 1,165 mg silicon/kg bw/day) was regarded as a NOAEL.

Exposure assessment

Total exposure/intake

Food up to 50 mg/day (Bowen and Peggs, 1984; Pennington, 1991)

Supplements up to 500 mg/day (Annex 4; OTC, 2001)

Water 10 mg/day (assuming 2 litres of water at maximum reported level of 5 mg/L) (Pennington, 1991)

Estimated maximum intake: 50 + 500 + 10 mg = 560 mg/day

No potential high intake groups were identified.

Risk assessment

Few data are available on oral silicon toxicity in humans.

Animal data are available on certain forms of silicon, which suggest that high levels of silicon in the form of silicates can reduce growth and alter mineral levels in rats and turkeys, fed 500 ppm (approximately 50 mg/kg bw) and 270 ppm silicon, from 3 silicon sources respectively. Some chronic studies investigating the food additive syloid (99% amorphous silicon dioxide) are also available. Reductions in growth rates and organ weights at the higher doses were reported but no significant effects on haematology or gross or microscopic pathology were observed. The changes reported may have been due to nutritional inadequacies in the diet. Overall it can be concluded that the chronic toxicity of silicon as amorphous silica is low.

Silica by inhalation is a known carcinogen, but this results from a mechanism specific to inhalation exposure. The available genotoxicity data are largely negative, although these are limited.

No vulnerable groups have been identified and no data on the effects of silicon on children have been identified.

ESTABLISHMENT OF SAFE UPPER LEVEL

Key study: Takizawa *et al.* (1988)

NOAEL: 50,000 ppm supplemental dietary silica, equivalent to 2500 mg/kg bw/day in rats, 7500 mg/kg bw/day in mice). The study in rats has been used to establish the safe upper level.

Uncertainty factors: 10 for inter-species variation
 10 for inter-individual variation

Safe Upper Level 2500/100 = 25 mg/kg bw/day supplemental silica (equivalent to
 for daily 1500 mg/day for a 60 kg adult)

Consumption over
 a lifetime:

In terms of elemental silicon, this is equivalent to a Safe Upper Level of 12 mg/kg bw/day or 700 mg/day for a 60 kg adult for supplemental silicon.

Few data are available on the oral toxicity of silicon in humans and they are inadequate for risk assessment. Therefore the animal data have been considered for this purpose. The study by Kayonga-Male and Jia (1999) in rats and turkeys suggested that short term intakes of 500 and 270 ppm dietary silicon respectively as silicates may result in reduced growth and other changes in mineral levels. This study used tetraethylorthosilicate (an organic silicon compound), sodium zeolite, which contains aluminium, and sodium silicate, which is the compound most representative of silicon in food. A more detailed, chronic study by Takizawa *et al* (1988) indicated that chronic intakes of diets containing 12,500 and 25,000 ppm amorphous silica (equivalent to 600 and 1900 mg elemental silicon/kg bw/day) were not associated with any adverse effect in rats and mice respectively. The study did not investigate mineral levels but it is likely that any significant effects attributable to mineral deficiency would have

become apparent during the course of the study or would have been observed in the pathological examination. The adverse effects noted at 50,000 ppm (transient reductions in growth rates in mice and reduced liver weights in female rats) were likely to be due to nutritional imbalance and are not considered relevant to human exposure. Silicon does not have significant genotoxic potential.

The Safe Upper Level of 700 mg/day for supplemental intake of elemental silicon has been derived from a chronic dietary study in rats where no relevant adverse effects were observed at doses of up to 50,000 ppm silica in the diet, corresponding to 2500 mg/kg bw/day. Uncertainty factors of 10 for inter-species variation and 10 for inter-individual variation have been applied. Assuming an estimated maximum intake of 60 mg silicon from food and water, a Safe Upper Level for total silicon intake of 60 + 700 = 760 mg/day can be estimated. This is equivalent to 13 mg/kg bw/day for a 60 kg adult

No groups particularly vulnerable to silicon toxicity have been identified.

References

- Bowen, H.J.M. and Peggs, A. (1984) Determination of the silicon content of food. *Journal of Science Food and Agriculture* **35**, 1225-1229.
- Kayonga-Male, H. and Jia, X (1999). Silicon bioavailability studies in young rapidly growing rats and turkeys fed semi-purified diets. A comparative study. *Biological Trace Element Research* **67**, 173-186.
- Pennington, J.A.T. (1990) Silicon in foods and diets. *Food Additives and Contaminants* **8**, 97-118.
- Takizawa, Y, Hirasawa, F, Noritomo, E, Aida, M, Tsunoda, H, Uesugi, S. (1988). Oral ingestion of syloid to mice and rats and its chronic toxicity and carcinogenicity. *Acta Medica et Biologica* **36**, 27-56.