Selenium

A maximum acceptable concentration of *0.01 mg/L (10 µg/L)* for selenium in drinking water has been established on the basis of health considerations. Food is the main source of intake of selenium for individuals who are not occupationally exposed; thus, toxic effects have most often been associated with food intake. A safe and adequate range of selenium intake of 0.05 to 0.2 mg per person per day has been recommended for adults, with correspondingly lower ranges for infants and children. Drinking water containing selenium at the maximum acceptable concentration would be the source of between 10 and 25 percent of total selenium intake; the maximum acceptable concentration is considered to provide a reasonable factor of safety from adverse effects of selenium.

General

In general, selenium is present in the environment in elemental form or in the form of selenide (Se^{2-}), selenate (SeO_4^{2-}), or selenite (SeO_3^{2-}). It is widely distributed in the Earth's crust at concentrations averaging 0.09 mg/kg and is found in trace quantities in most plant and animal tissues.[1]

Concentrations of selenium in minerals are too low to allow its extraction alone to be economically feasible. Selenium is produced in Canada from copper refinery slimes and from flue dusts from copper smelters. A significant amount of selenium is also re-refined in Canada from xerographic scrap and other selenium scrap imported from the United States and other countries and then re-exported as the pure product. The production of selenium in all forms from Canadian refineries in 1983 was 352 tonnes; domestic consumption was 11.8 tonnes. Canada exports most of its production to the United States and Britain. Canada, the United States, and Japan are the world's major producers. Selenium is used in the manufacture of pigmented glass, stainless steel, electronic components (semi-conductors, photoelectric cells), explosives, batteries, animal and poultry feeds, pigments, fungicides, and certain medicines, and in xerography.[2]

Occurrence

All of the common oxidation states of selenium are found in the environment: selenides (-2), selenium (0), selenites (+4), and selenates (+6). The identity and proportions of the various oxidation-state species in soils (the primary source of environmentally distributed selenium) depend on redox-potential conditions — lower oxidation states predominate in poorly aerated, acidic soils, and the higher oxidation states are favoured in alkaline, well-aerated soils. Both selenites and selenates are taken up by plants (the major point of entry of selenium into the human food chain), where they are converted to protein-bound selenomethionine, soluble inorganic forms, several free amino acids, and volatile organoselenium compounds. The selenates, however, are considered the most readily available to plants. The elemental form of selenium has appreciable volatility and hence will enter the atmospheric environmental compartment, as will selenium dioxide (for example, in emissions from smelting operations and coal burning) and volatile organoselenium compounds produced by plants. Selenium occurs in natural waters in trace amounts as a result of geochemical processes, such as weathering of rocks and erosion of soils, and is usually present in water as selenate or selenite; however, the elemental form may be carried in suspension.[3,4]

The concentration of selenium measured in Canadian surface water ranges from non-detectable ($<0.1 \times 10^{-4}$ mg/L) to 4×10^{-3} mg/L.[5] Studies of selenium in rivers in the Great Lakes basin indicate that concentrations are lower in lakes and rivers geographically isolated from large urban centres, and this has been interpreted as an indication that atmospheric pollution may contribute substantially to selenium contamination of natural waters.[6] A mean selenium concentration of 2×10^{-4} mg/L has been recorded for natural waters in the United States.[7]

A 1982 survey of drinking water supplies from 122 municipalities across Canada (representing 36 percent of the Canadian population) showed that selenium was present at or below the detection limit of 5×10^{-4} mg/L (raw, treated, and distributed water samples were analysed).[8] Higher selenium concentrations may, however, be encountered in some Canadian drinking water. An earlier (1975) study of 120 Manitoba

drinking water supplies found that, whereas 93 percent had concentrations below 5×10^{-3} mg/L (the detection limit), 7 percent had concentrations between 0.005 and 0.01 mg/L.[9]

There is no information available on levels of selenium in the air of Canadian communities. In the United States, it has been estimated that the average selenium concentration in air is 10^{-6} mg/m^3.[10] In urban centres, levels are somewhat higher due to stack emissions from incinerators. Bennett has estimated that a representative concentration of selenium in urban atmospheres would be 3×10^{-6} mg/m^3 (range, 10^{-8} to 3×10^{-5} mg/m^3), whereas that in rural atmospheres would be 1.3×10^{-6} mg/m^3 (range, 10^{-8} to 3×10^{-6} mg/m^3).[11]

Analysis of selenium in Canadian foods has revealed that concentrations in milk range from 5×10^{-6} to 6×10^{-5} mg/g and those in cereals range from 8×10^{-5} to 1.3×10^{-3} mg/g; concentrations average 3×10^{-5} mg/g in meat and 5×10^{-5} mg/g in vegetables.[12] Concentrations between 10^{-5} and 8×10^{-5} mg/g have been recorded in fish from Lake Erie and Lake Ontario;[6] an average concentration of 3.3×10^{-3} mg/g in freshwater fish from central Canada has been recorded.[13] The marked variation in the selenium content of some foods is due largely to the variable distribution of selenium in soils. Cooking or food processing has little effect on the selenium content of foods.[14]

Canadian Exposure

Based on analysis of prepared foods, the daily intake of selenium in typical Canadian diets has been estimated to be 0.191 mg in Winnipeg, 0.224 mg in Halifax, and 0.113 mg and 0.149 mg in Toronto.[15] Somewhat lower selenium intakes were measured in the diets of 84 Canadian women; a mean value of 0.077 mg/day was found, with a range of 0.031 to 0.166 mg/day.[16] These values compare with the results from total-diet studies in the United States, which showed (for the year 1981/82, the latest period for which figures are available) that the average adult intake was 0.139 mg/day,[17] whereas those for toddlers and infants were 0.054 and 0.022 mg/day, respectively.[18]

Assuming individual daily water consumption to be 1.5 L[19] and the selenium content of Canadian drinking water measured by Subramanian and Méranger to be less than 5×10^{-4} mg/L, then the average daily intake from drinking water would be less than 10^{-3} mg per person. Compared with food, therefore, drinking water makes a negligible contribution to total selenium intake. Even more negligible is the contribution to total daily intake made by selenium in air. If Bennett's estimates of 3×10^{-6} mg/m^3 for selenium in urban air and 1.3×10^{-6} mg/m^3 for selenium in rural air[11] are assumed to apply in Canada, and if the daily respiratory volume is assumed to be 20 m^3, then the daily intake of selenium from the atmosphere would be 6×10^{-5} and 2.6×10^{-5} mg for urban and rural populations, respectively.

These data suggest that the total daily intake of selenium from food, air, and water for Canadian adults would be in the range of 0.05 to 0.2 mg; children would have lower intakes. More than 98 percent of these intakes would come from food.

Treatment Technology[20]

Laboratory experiments and pilot-plant studies have shown that alum and ferric sulphate coagulation and lime softening are ineffective in removing selenates (Se^{6+}) from water and are only moderately successful in removing selenites (Se^{4+}). Of the two coagulants, ferric sulphate is the more effective in removing selenites. Removal efficiency is, however, very dependent on pH; below pH 5.5, 85 percent removal can be achieved, but this drops to 15 percent at pH 9.2. Alum coagulation removes no more than 20 to 30 percent over this pH range. Removal of selenites by lime softening increases with increasing pH, but the maximum that can be achieved is only 45 percent (and only at a pH of 11.5).

Very limited laboratory tests have demonstrated that both ion exchange and reverse osmosis can be very effective in removing selenates and selenites from water. Better than 97% removal was obtained in solutions containing about 0.1 mg/L of selenium (as either Se^{6+} or Se^{4+}).

Health Considerations

Essentiality

Following earlier conclusions that selenium is an essential element in animal nutrition,[21,22] there is now consensus that it is also an essential trace element in the human diet.[11,23–25] The most persuasive evidence for essentiality in humans comes from the association of Keshan disease (a juvenile cardiomyopathy endemic in certain areas of China) with selenium deficiency in the diet.[26,27] This disease is limited to those areas of China where, because the selenium content of soils is low, dietary intakes of selenium are less than 0.03 mg/day. The condition is characterized by heart enlargement, abnormal electrocardiograms, cardiogenic shock, and congestive heart failure. The disease is mainly seen in rural areas and occurs predominately in agricultural inhabitants (peasants and their families), the most susceptible being children from 2 to 15 years of age and women of child-bearing age. It was found that the administration of sodium selenite (0.5 mg weekly for 1 to 5 year olds and 1.0 mg weekly for 6 to 9 year olds)

essentially eliminated the disease in a previously afflicted geographical area. A note of caution has, however, been sounded by Guanquing, with the suggestion that Keshan disease may result from a viral infection, the effects of which are exacerbated by selenium deficiency or by a combination of low selenium and low protein intakes.[28] There have also been reports of conditions in individuals that have responded to the administration of supplementary selenium: relief of symptoms of muscular discomfort in a patient on long-term total parenteral nutrition in New Zealand[29] and the treatment of cardiomyopathy in a selenium-deficient patient in the United States.[30]

Selenium has been shown in *in vitro* culture studies to increase the growth of human fibroblasts,[31] and it occurs in the enzyme glutathione peroxidase isolated from human erythrocytes.[32] Glutathione peroxidase appears to interact with vitamin E in protecting the cell membrane against oxidative destruction,[16] and Thompson and Robinson have suggested that it is for this reason that selenium is required for the clonal growth of human fibroblasts.[33]

Ingestion

Barbezat *et al.* have pointed out in a recent review that absorption of selenium has not been studied extensively in man.[34] Much of the work has been carried out in their own laboratory and involved New Zealand residents who, as a national group, tend to have low intake and low body content of selenium. These researchers found the actual extent of selenium absorption depended on the nature of the selenium-containing matrix: selenomethionine (a naturally occurring selenium-containing amino acid) was more completely absorbed than inorganic selenites (species more likely to be found in drinking water than organoselenium compounds) — 80 to 90 percent and 60 to 70 percent, respectively — with food selenium (which comprises both organic and inorganic selenium compounds) intermediate between the two. Coupled with this ready absorption of selenium is an endogenous excretion, and thus the apparent uptake appears lower (about 75 percent for selenomethionine and between 46 and 61 percent for selenite). Similar results, also reviewed by Barbezat *et al.*, were obtained in U.S. subjects[35–37] and in Germans,[38] all individuals who normally had higher natural intakes of selenium in their diets than the New Zealanders.

Sunde has postulated that selenium is metabolized by a combination of reduction and methylation processes via an intermediate, inorganic selenide compound (HSe^-).[39] Selenium is excreted by mono-gastric mammals (including man) mainly in faeces and urine, with a minor route through the lungs (as dimethylselenide); the relative importance of these three routes depends on the nature of the selenium compound being ingested and on the magnitude and duration of the dose. (For a review of excretory pathways, see reference 40.) The major urinary metabolite of selenium is the trimethyl-selenonium ion. The amount of selenium excreted in urine is loosely related to the amount of selenium in the diet.

It is difficult to draw conclusions about quantities of selenium that are toxic, because of a number of complicating factors. The quantity and nature of protein in the diet[34,35] and the presence of vitamin E[41–44] modify the toxicity of selenium. Health effects are also dependent upon the chemical form of selenium; elemental selenium is inert and generally considered non-toxic. As well, metabolic interrelationships exist between selenium and such elements as arsenic,[45–49] cadmium,[50,51] mercury,[50,52–56] lead,[57,58] silver,[56,59–63] and thallium;[64,65] in some cases the toxicities of selenium and these other elements are antagonistic, whereas in others they are synergistic.[21] The biochemical bases for these interactions are largely unknown. Nonetheless, estimates of 0.5[66] and 0.7[34] mg/day have been made for the minimum daily intake of selenium likely to give rise to toxic effects in humans.

Most toxic effects of selenium appear to be associated with the consumption of selenium at high concentrations in food rather than in drinking water, and there is some evidence that chronic selenium toxicity of dietary origin occurs in man. High daily intake of selenium in the diet of humans (0.1 to 0.2 mg/kg body weight) has been correlated with jaundice, chloasma, vertigo, chronic gastrointestinal disease, dermatitis, nail changes, lassitude, and fatigue.[67,68] Consumption of drinking water with a selenium concentration of 9 mg/L for three months resulted in loss of hair, weakened nails, and listlessness in several individuals.[69] More recently, a group of Venezuelan children living in seleniferous areas was compared with a control group.[70] The selenium levels in blood of children in seleniferous areas was more than double those of the control group, but the only signs to correlate with blood or urinary selenium were the somewhat poorly defined clinical findings of nausea and pathological nails.

The human symptoms of selenosis described above are similar, in general terms, to those observed in domestic animals suffering chronic selenosis from grazing on land with highly seleniferous soil.[21] In laboratory animals, ingestion of drinking water with a selenite concentration of 0.01 mg/L results in decreased liver function in rabbits.[71] This result is somewhat questionable, because the selenium content of the diet was not quantified, and the results from the liver function test may not have been reliable. In another study, a small reduction in the rate of weight gain was noted when 2 to 3 mg selenium per litre as selenite and selenate was administered in drinking water for six weeks to rats on corn-based or rye-based diets.[72] A

similar study had previously shown that toxic symptoms in rats occurred from ingestion of selenium (as selenite) at a concentration of 3 mg/L in drinking water, but not with ingestion of similar levels of selenate.[73]

Other Routes

Very little quantitative information is available on the absorption of selenium compounds through the lungs or skin. Comparatively little absorption occurs after local application of selenium sulphide to normal skin. The compound, which is contained in some anti-dandruff shampoos, is absorbed more readily by an inflamed or damaged epithelium.[74] Industrial exposure to elemental selenium, hydrogen selenide, or selenium oxychloride through the skin or lungs has resulted in pallor, nervousness, depression, dermatitis, gastro-intestinal disturbances, and garlic odour of the breath.[21]

Carcinogenicity

The carcinogenic potential of selenium has been widely investigated in both laboratory and epidemiological studies, and there is much conflicting information on the subject. (See, for example, the reviews and assessments by the International Agency for Research on Cancer,[75] Schrauzer,[76] the U.S. National Academy of Sciences,[21] the U.S. Environmental Protection Agency,[40] and Diplock.[77]) The consensus is that the available animal data are insufficient to allow an evaluation of the carcinogenicity of selenium compounds, and that available human data provide no suggestion that selenium is carcinogenic in man. There is, however, evidence that selenium is mutagenic at the molecular and cellular levels *in vitro*.[78,79] Selenium has also been shown to be teratogenic in a number of avian and mammalian species (a subject extensively reviewed by the U.S. National Academy of Sciences[21]), and there have been suggestions that selenium may also be a teratogen in humans.[80,81]

Data from epidemiological and laboratory studies suggest that selenium may have anti-carcinogenic properties.[21,75,82,83] There is some indication that the incidence of human cancer mortality is inversely related to the amounts of selenium in the environment, to dietary intake, and to levels of selenium in the blood.[83–85] These studies should be viewed with some caution; for example, the International Agency for Research on Cancer has concluded "that the evidence for a negative correlation between regional cancer death rates and selenium is not convincing",[75] and Robinson has stated, "We are convinced from our New Zealand studies that cancer is not caused by selenium deficiency *per se*, but that the low selenium status of our patients was more a consequence of the illness".[23] Selenium has, however, been shown to have inhibitory effects on chemically induced carcinogenesis in rodent species.[21,75]

Cardiovascular Disease

There are some epidemiological data that suggest a connection between low selenium intakes or blood levels and cardiovascular disease. Shamberger *et al*. have reported that the death rate from atherosclerotic heart disease is lower in areas with selenium-rich soil.[86] A case-control epidemiological study in Finland (a geographical area with generally low levels of soil selenium) has shown that the relative risks of coronary heart disease death, cardiovascular death, and fatal and non-fatal myocardial infarction were all more than twice as high ($p < 0.01$) among individuals having serum selenium concentrations below 0.045 mg/L.[87] A recent study of dietary intake of selenium in three rural communities in northern Italy that have a high death rate for coronary heart disease showed that the average adult intake of selenium was 0.043 mg/day, a value lower than the 0.05 to 0.2 mg/day considered adequate for healthy adults.[88]

Acceptable Daily Intake

In the last 10 years or so, considerable advances have been made regarding the role selenium plays in human health, but the picture is still far from clear.[11,23–25,77] Robinson, for example, has pointed out that "the margin between deficiency and toxicity seems narrower for Se than for some other trace elements" and adds, "to serve as a warning against marginal or excessive intake of Se, the U.S. Food and Nutrition Board have recommended for the first time a range of adequate and safe intakes".[23] The safe and adequate range established by this board has been set at 0.05 to 0.2 mg per person per day for adults, with correspondingly lower ranges for infants and children.[89] The dietary requirement below which adverse health effects may occur has been variously and tentatively estimated to be 0.02 to 0.12 mg/day,[21,90] and the minimum toxic selenium intake has been variously estimated at 0.5[66] or 0.7[88] mg/day.

Rationale

1. It is now reasonably well established that selenium is an essential element in human nutrition. It is unclear whether or not selenium can be considered a carcinogen. Studies have indicated that selenium might have anti-carcinogenic properties. Ingestion of large amounts of selenium has been correlated with a variety of clinical disorders in humans, as has ingestion of insufficient quantities of selenium.

2. Food is the main source of intake of selenium for humans who are not occupationally exposed, and toxic effects are most often associated with its intake in food. There is little information available on the toxicity of selenium in drinking water. The minimum toxic intake level has been identified for adults as 0.5 to 0.7 mg/day, and daily intakes of less than 0.02 or 0.03 mg may also

be linked to adverse health effects. The U.S. National Academy of Sciences has recommended a safe and adequate range of 0.05 to 0.2 mg per person per day for adults, with correspondingly lower ranges for infants and children.

3. The maximum acceptable concentration of selenium in drinking water is 0.01 mg/L. If selenium is present at this level, drinking water would be the source of between 10 and 25 percent of total selenium intake.

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