Selenium in Drinking-water

Background document for development of WHO Guidelines for Drinking-water Quality

Preface

One of the primary goals of WHO and its member states is that “all people, whatever their stage of development and their social and economic conditions, have the right to have access to an adequate supply of safe drinking water.” A major WHO function to achieve such goals is the responsibility “to propose regulations, and to make recommendations with respect to international health matters ....”

The first WHO document dealing specifically with public drinking-water quality was published in 1958 as International Standards for Drinking-Water. It was subsequently revised in 1963 and in 1971 under the same title. In 1984–1985, the first edition of the WHO Guidelines for drinking-water quality (GDWQ) was published in three volumes: Volume 1, Recommendations; Volume 2, Health criteria and other supporting information; and Volume 3, Surveillance and control of community supplies. Second editions of these volumes were published in 1993, 1996 and 1997, respectively. Addenda to Volumes 1 and 2 of the second edition were published in 1998, addressing selected chemicals. An addendum on microbiological aspects reviewing selected microorganisms was published in 2002.

The GDWQ are subject to a rolling revision process. Through this process, microbial, chemical and radiological aspects of drinking-water are subject to periodic review, and documentation related to aspects of protection and control of public drinking-water quality is accordingly prepared/updated.

Since the first edition of the GDWQ, WHO has published information on health criteria and other supporting information to the GDWQ, describing the approaches used in deriving guideline values and presenting critical reviews and evaluations of the effects on human health of the substances or contaminants examined in drinking-water.

For each chemical contaminant or substance considered, a lead institution prepared a health criteria document evaluating the risks for human health from exposure to the particular chemical in drinking-water. Institutions from Canada, Denmark, Finland, France, Germany, Italy, Japan, Netherlands, Norway, Poland, Sweden, United Kingdom and United States of America prepared the requested health criteria documents.

Under the responsibility of the coordinators for a group of chemicals considered in the guidelines, the draft health criteria documents were submitted to a number of scientific institutions and selected experts for peer review. Comments were taken into consideration by the coordinators and authors before the documents were submitted for final evaluation by the experts meetings. A “final task force” meeting reviewed the health risk assessments and public and peer review comments and, where appropriate, decided upon guideline values. During preparation of the third edition of the GDWQ, it was decided to include a public review via the world wide web in the process of development of the health criteria documents.

During the preparation of health criteria documents and at experts meetings, careful consideration was given to information available in previous risk assessments carried out by the International Programme on Chemical Safety, in its Environmental Health
Criteria monographs and Concise International Chemical Assessment Documents, the International Agency for Research on Cancer, the joint FAO/WHO Meetings on Pesticide Residues, and the joint FAO/WHO Expert Committee on Food Additives (which evaluates contaminants such as lead, cadmium, nitrate and nitrite in addition to food additives).

Further up-to-date information on the GDWQ and the process of their development is available on the WHO internet site and in the current edition of the GDWQ.
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GENERAL DESCRIPTION

Identity

Selenium is present in the earth's crust, often in association with sulfur-containing minerals. It can assume four oxidation states (-2, 0, +4, +6) and occurs in many forms, including elemental selenium, selenites and selenates (1).

Physicochemical properties (1)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical state</td>
<td>Grey metallic/red amorphous powder or vitreous form</td>
</tr>
<tr>
<td>Boiling point</td>
<td>685 °C</td>
</tr>
<tr>
<td>Water solubility</td>
<td>Insoluble</td>
</tr>
</tbody>
</table>

Organoleptic properties

Many selenium compounds are odoriferous, some having an odour of garlic (1).

Environmental fate

Acid and reducing conditions reduce inorganic selenites to elemental selenium, whereas alkaline and oxidizing conditions favour the formation of selenates. Selenites and selenates are usually soluble in water. Elemental selenium is insoluble in water and not rapidly reduced or oxidized in nature. In alkaline soils, selenium is present as water-soluble selenate and is available to plants; in acid soils, it is usually found as selenite bound to iron and aluminium oxides in compounds of very low solubility (2).

ANALYTICAL METHODS

Atomic absorption spectrometry with hydride generation is the most convenient method of determining selenium in drinking-water. If 10-ml samples are used for routine analysis, the detection limit is about 0.5 µg/litre. Lower levels can be determined if larger sample volumes are used (3).

ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

Air

The level of selenium (mostly bound to particles) in most urban air ranges from 0.1 to 10 ng/m³, but higher levels may be found in certain areas, e.g. in the vicinity of copper smelters (4).

Water

The levels of selenium in groundwater and surface water range from 0.06 to about 400 µg/litre (5–7); in some areas, levels in groundwater may approach 6000 µg/litre (8). Concentrations increase at high and low pH as a result of conversion into compounds of greater solubility in water. Levels of selenium in tapwater samples from public water supplies around the world are usually much less than 10 µg/litre (9,10). Drinking-water from a high-selenium area in China was reported to contain 50–160 µg/litre (1).
Vegetables and fruits are mostly low in selenium content (<0.01 mg/kg). Levels of selenium in meat and seafood are about 0.3–0.5 mg/kg. Grain and cereal products usually contain <0.01–0.67 mg/kg. Great variations in selenium content have been reported in China, where those of corn, rice, and soya beans in high- and low-selenium areas were 4–12 and 0.005–0.01 mg/kg, respectively (1,2).

**Estimated total exposure and relative contribution of drinking-water**

Foodstuffs constitute the main source of selenium for the general population. Daily dietary intake varies considerably according to geographical area, food supply, and dietary habits. Recommended daily intakes have been set at 1.7 µg/kg of body weight in infants and 0.9 µg/kg of body weight in adults (11).

Most drinking-water contains much less than 10 µg/litre, except in certain seleniferous areas. A level of 1 µg/litre corresponds to an intake of 2 µg of selenium per day. Thus, given an intake from food of about 60 µg/day, the relative contribution from drinking-water is small. Even in high-selenium areas, the relative contribution of selenium from drinking-water may be small in comparison with that from locally produced food (1).

The intake of selenium by the general population from air and smoking appears to be insignificant and has been estimated to be less than 1–2 µg/day (12).

**KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS**

Most water-soluble selenium compounds and selenium from food are effectively absorbed in the gastrointestinal tract (13). Elemental selenium (14) and selenium sulfide (15) are poorly absorbed. After absorption, water-soluble selenium compounds appear to be rapidly distributed to most organs, the highest concentrations being in kidney, liver, spleen, and testes (16,17).

Selenium compounds are biotransformed into excretable metabolites, including unknown as well as methylated selenides and trimethylselenonium ion at higher doses (1,12,13,18). Selenides may react with metals in the body to form metal selenides (12). Most (49–70%) selenium is excreted in urine (19). In humans, selenite is eliminated in three phases, with half-lives of 1, 8–20, and 100 days, respectively (13).

Selenium is an essential trace element for many species, including humans (2,11,20). It is incorporated into proteins via a specific selenocysteine tRNA with co-translational synthesis of selenocysteine from phosphoserine tRNA and inorganic selenium (20,21). Selenium is found as selenocysteine in glutathione peroxidase (2,20) and is incorporated into other proteins, such as tetraiodothyronine deiodinase and selenoprotein P (20,22,23). (-)-Selenomethionine from food is apparently nonspecifically incorporated in proteins in competition with (-)-methionine.

**EFFECTS ON LABORATORY ANIMALS AND IN VITRO TEST SYSTEMS**

**Acute exposure**

Selenite, selenate, selenocysteine, and selenomethionine are highly toxic and kill laboratory animals in single doses of 1.5–6 mg/kg of body weight (1,12).
Long-term exposure

Signs of selenium deficiency in many farm and laboratory animals include degenerative changes of several organs, growth retardation, and failure to reproduce (2,24).

In rats, 5 mg of selenium per kg of diet may result in growth reduction (25,26). At a dietary level of 6.4 mg of selenium per kg (given as selenite), liver changes and splenomegaly occurred. At 8 mg of selenium per kg, anaemia, pancreatic enlargement, and increased mortality were observed (25). Based on growth retardation, apparently caused by reduced secretion of growth hormone from the anterior pituitary gland as a result of local selenium accumulation (27), a NOAEL of about 0.4 mg of selenium per kg of body weight per day was suggested. Hepatotoxic effects have also been described following dietary administration of selenium (28,29). Based on both growth retardation and organ toxicity, a LOAEL of 0.03 mg/kg of body weight per day has been suggested.

The syndromes "blind staggers" and "alkali disease" have been described in livestock and are associated with the consumption of selenium in accumulator plants (30).

Reproductive toxicity, embryotoxicity, and teratogenicity

Selenate, selenite, and the amino acids selenocysteine and selenomethionine are teratogenic in avian species (31) and fish (32). Teratogenicity has also been observed in sheep (33) and pigs (34). In recent studies on monkeys (Macaca fascicularis) fed selenomethionine (25, 150 or 300 µg/kg of body weight per day) during organogenesis, no signs of teratogenicity were observed (35).

Adverse effects of selenate (3 mg/litre in drinking-water) on reproduction in mice and rats have been reported (36), but there are also two negative reports on the effects of selenite in hamsters and mice (37). Only at doses associated with overt maternal poisoning and nutritional deprivation was evidence of selenomethionine-induced embryonic or fetal toxicity observed in rabbits and hamsters (38,39).

Mutagenicity and related end-points

A weak base-pair substitution mutagenic activity has been demonstrated for both selenite and selenate in Salmonella typhimurium strain TA100 (40,41). Selenite, selenate, and selenide induced unscheduled DNA synthesis, sister chromatid exchange, and chromosomal aberrations in cell cultures in vitro, often in the presence of glutathione (42–44). In one in vivo study, chromosomal aberrations and increased sister chromatid exchange were seen in hamster bone marrow cells after selenite treatment, but only at toxic doses (45).

Carcinogenicity

Early studies in which tumours were seen in test animals (46,47) have been seriously questioned because of study limitations (48), and several evaluators have found the data to be inconclusive. In two studies on mice, there was either no increase or a decrease in the incidence of tumours after the administration of selenite or selenate (3 mg of selenium per litre of drinking-water) (49) or selenium oxide (2 mg of selenium per litre of drinking-water) (50). Further data indicate an anticarcinogenic effect of selected selenium compounds. Viewed collectively, these data seem to show that the compounds studied will not act as carcinogens at low or moderate doses (12).

Selenium sulfide given by gavage resulted in hepatocellular carcinomas in rats and mice (51) but caused no increased incidence in tumours when applied to the skin of mice (52).
EFFECTS ON HUMANS

In humans, few reports of clinical signs of selenium deficiency are available. It has been suggested that it may be a factor in endemic cardiomyopathia (Keshan disease) and possibly also in the joint and muscle disease (Kaschin-Beck disease) in the Keshan region of China (1,12).

Acute oral doses of selenite and other selenium compounds cause symptoms such as nausea, diarrhoea, abdominal pain, chills, tremor, numbness in limbs, irregular menstrual bleeding, and marked hair loss (12,53).

High dietary intakes of selenium have been investigated in selenium-rich areas of South Dakota, USA (54). Symptoms in people with high urinary selenium levels included gastrointestinal disturbances, discoloration of the skin, and decayed teeth (54).

Children living in a seleniferous area in Venezuela exhibited more pathological nail changes, loss of hair, and dermatitis than those living in Caracas (55). Based on Chinese data on blood level–intake relationships (56), their estimated daily intake was about 0.66 mg of selenium. However, the groups concerned differed nutritionally in several ways.

In China, endemic selenium intoxication has been studied by Yang and colleagues (57). Morbidity was 49% among 248 inhabitants of five villages where the daily intake was about 5 mg of selenium. The main symptoms were brittle hair with intact follicles, lack of pigment in new hair, thickened and brittle nails, and skin lesions. Symptoms of neurological disturbances were observed in 18 of the 22 inhabitants of one heavily affected village only. Those affected recovered once diets were changed following evacuation from the areas concerned.

In a follow-up study, Yang et al. studied a population of about 400 individuals with average daily intakes ranging from 62 to 1438 µg (56,58). Clinical signs of selenosis (hair or nail loss, nail abnormalities, mottled teeth, skin lesions, and changes in peripheral nerves) were observed in 5 of 439 adults having a mean blood selenium of 1346 µg/litre, corresponding to a daily intake of 1260 µg of selenium. A decrease in prothrombin time and in the concentration of glutathione in blood were seen at dietary intakes exceeding 750–850 µg.

In a recent study, 142 subjects from geographical areas where the average selenium intake was 239 µg/day (68–724 µg/day) were examined over 2 years (59). An association between selenium intake and alanine aminotransferase (ALAT) levels in serum was observed but considered to be clinically insignificant. None of the effects, including nail abnormalities, were related to selenium intake.

One case of selenium toxicity directly attributable to a water source has been reported. A family was exposed for about 3 months to well-water containing 9 mg of selenium per litre. They suffered from loss of hair, weakened nails, and mental symptoms, but recovered when they stopped using the water from the well concerned (33).

Two individuals received about 350 and 600 µg of selenium per day via diet and selenium-containing yeast for 18 months. Marginal haematological changes and a borderline increase in ALAT levels were seen (60). In a small group of patients with rheumatoid arthritis receiving daily supplements of 250 µg of selenium in selenium-enriched yeast in addition to selenium from food for 6 months, levels of selenium in serum and erythrocytes were increased considerably in comparison with those in a group receiving placebo (61).
GUIDELINE VALUE

Except for selenium sulfide, which does not occur in drinking-water, selenium does not appear to be carcinogenic. IARC has placed selenium and selenium compounds in Group 3 (62). Selenium compounds have been shown to be genotoxic in in vitro systems with metabolic activation. There was no evidence of teratogenic effects in monkeys. Long-term exposure in rats may result in growth retardation and liver pathology.

In humans, the toxic effects of long-term selenium exposure are manifested in nails, hair, and liver. Data from Chinese indicate that clinical and biochemical (decreased liver prothrombin synthesis) signs occur at a daily intake above 0.8 mg. Daily intakes by Venezuelan children with clinical signs were estimated at about 0.66 mg on the basis of their blood levels and the Chinese data on the relationships between blood level and intake. Effects on the synthesis of a liver protein were also seen in a small group of patients with rheumatoid arthritis given selenium at a rate of 0.25 mg/day (total daily intake from all sources about 0.35 mg). No clinical or biochemical signs of selenium toxicity were reported in a group of 142 persons with a mean daily intake of 0.24 mg (maximum 0.72 mg) from food. However, the liver enzyme ALAT was positively correlated within reference values with selenium intake.

On the basis of these data, the NOAEL in humans was estimated to be about 4 µg/kg of body weight per day, on the assumption that soluble selenium salts in drinking-water may be more toxic than organic-bound selenium in food. The recommended daily intake of selenium is 0.9 µg/kg of body weight for adults. An allocation of 10% of the NOAEL in humans to drinking-water gives a health-based guideline value of 0.01 mg/litre (rounded figure).

REFERENCES

38. Berschneider F et al. [Fetal and maternal damage to rabbits following application of sodium selenite, injectable Ursoselevit, and Ursoselevit premix.] *Monatshefte für Veterinärmedizin*, 1977, 8:299-304 (in German).