1. General description

Identity

Silver (CAS no. 7440-22-4) is present in silver compounds primarily in the oxidation state +1 and less frequently in the oxidation state +2. A higher degree of oxidation is very rare. The most important silver compounds from the point of view of drinking-water are silver nitrate (AgNO₃, CAS no. 7761-
88-8) and silver chloride (AgCl, CAS no. 7783-90-6).

**Physicochemical properties (1)**

<table>
<thead>
<tr>
<th>Property</th>
<th>AgNO₃</th>
<th>AgCl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colour</td>
<td>White</td>
<td>White, darkens when exposed to light</td>
</tr>
<tr>
<td>Melting point (°C)</td>
<td>212</td>
<td>455</td>
</tr>
<tr>
<td>Water solubility at 25 °C (g/litre)</td>
<td>2150</td>
<td>0.00186</td>
</tr>
</tbody>
</table>

**Major uses**

The electrical and thermal conductivity of silver are higher than those of other metals. Important alloys are formed with copper, mercury, and other metals. Silver is used in the form of its salts, oxides, and halides in photographic materials and alkaline batteries, or as the element in electrical equipment, hard alloys, mirrors, chemical catalysts, coins, table silver, and jewellery. Soluble silver compounds may be used as external antiseptic agents (15–50 μg/litre), as bacteriostatic agents (up to 100 μg/litre), and as disinfectants (>150 μg/litre) (2).

**Environmental fate**

Silver occurs in soil mainly in the form of its insoluble and therefore immobile chloride or sulfide. As long as the sulfide is not oxidized to the sulfate, its mobility and ability to contaminate the aquatic environment are negligible. Silver in river water is "dissolved" by complexation with chloride and humic matter (3).

**2. Analytical methods**

The detection limit of the spectrographic and colorimetric method with dithizone is 10 μg of silver per litre for a 20-ml sample. The detection limit of atomic absorption spectroscopy (graphite furnace) is 2 μg of silver per litre, and of neutron activation analysis, 2 ng of silver per litre (4).

**3. Environmental levels and human exposure**

**Air**

Ambient air concentrations of silver are in the low nanogram per cubic metre range (5).

**Water**
**Water**

Average silver concentrations in natural waters are 0.2–0.3 µg/litre. Silver levels in drinking-water in the USA that had not been treated with silver for disinfection purposes varied between “non-detectable” and 5 µg/litre. In a survey of Canadian tapwater, only 0.1% of the samples contained more than 1–5 ng of silver per litre (3). Water treated with silver may have levels of 50 µg/litre or higher (4); most of the silver will be present as nondissociated silver chloride.

**Food**

Most foods contain traces of silver in the 10–100 µg/kg range (6).

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

The median daily intake of silver from 84 self-selected diets, including drinking-water, was 7.1 µg (6). Higher figures have been reported in the past, ranging from 20 to 80 µg of silver per day (7). The relative contribution of drinking-water is usually very low. Where silver salts are used as bacteriostatic agents, however, the daily intake of silver from drinking-water can constitute the major route of oral exposure.

4. **Kinetics and metabolism in laboratory animals and humans**

Silver may be absorbed via the gastrointestinal tract, lungs, mucous membranes, and skin lesions (5). The absorption rate of colloidal silver after oral application can be as high as 5% (8). Most of the silver transported in blood is bound to globulins (5). In tissues, it is present in the cytosolic fraction, bound to metallothionein (9). Silver is stored mainly in liver and skin and in smaller amounts in other organs (5, 10). The biological half-life in humans (liver) ranges from several to 50 days (9).

The liver plays a decisive role in silver excretion, most of what is absorbed being excreted with the bile in the faeces. In mice, rats, monkeys, and dogs, cumulative excretion was in the range 90–99%. Silver retention was about 10% in the dog, <5% in the monkey, and <1% in rodents (10). In humans, under normal conditions of daily silver exposure, retention rates between 0 and 10% have been observed (5).

5. **Effects on laboratory animals and in vitro test systems**

**Acute exposure**

Oral LD$_{50}$ values between 50 and 100 mg/kg of body weight have been observed for different silver salts in mice (11).

**Short-term exposure**

Hypoactive behaviour was observed in mice that had received 4.5 mg of silver
Hypoactive behaviour was observed in mice that had received 4.5 mg of silver per kg of body weight per day for 125 days (12).

**Long-term exposure**

After 218 days of exposure, albino rats receiving approximately 60 mg of silver per kg of body weight per day via their drinking-water exhibited a slight greyish pigmentation of the eyes, which later intensified (13). Increased pigmentation of different organs, including the eye, was also observed in Osborne-Mendel rats after lifetime exposure to the same dose (14). Antagonistic effects between silver and selenium, involving the selenium-containing enzyme glutathione peroxidase, were observed in Holtzman rats (15).

**Mutagenicity and related end-points**

In the *rec*-assay with *Bacillus subtilis*, there were no indications that silver chloride was mutagenic (16). Reverse mutations in *Escherichia coli* were not induced by silver nitrate (17). In the DNA repair test with cultivated rat hepatocytes, silver nitrate solution was positive only at a moderately toxic concentration (18). Silver nitrate increased the transformation rate of SA7-infected embryonic cells of Syrian hamsters (19).

**Carcinogenicity**

Silver dust suspended in trioctanoin injected intramuscularly in Fischer 344 rats of both sexes was not carcinogenic (20).

**6. Effects on humans**

The estimated acute lethal dose of silver nitrate is at least 10 g (21).

The only known clinical picture of chronic silver intoxication is that of argyria, a condition in which silver is deposited on skin and hair, and in various organs following occupational or iatrogenic exposure to metallic silver and its compounds, or the misuse of silver preparations. Pigmentation of the eye is considered the first sign of generalized argyria (21). Striking discoloration, which occurs particularly in areas of the skin exposed to light, is attributed to the photochemical reduction of silver in the accumulated silver compounds, mainly silver sulfide. Melanin production has also been stimulated in some cases (22,23).

It is difficult to determine the lowest dose that may lead to the development of argyria. A patient who developed a grey pigmentation in the face and on the neck after taking an unknown number of anti-smoking pills containing silver ethanoate was found to have a total body silver content of 6.4 ± 2 g (22). It has been reported that intravenous administration of only 4.1 g of silver arsphenamine (about 0.6 g of silver) can lead to argyria (24). Other investigators concluded that the lowest intravenous dose of silver arsphenamine causing argyria in syphilis patients was 6.3 g (about 0.9 g of
arsphenamine causing argyria in syphilis patients was 6.3 g (about 0.9 g of silver) (21). It should be noted that syphilis patients suffering from argyria were often already in a bad state of health and had been treated with bismuth, mercury, or arsphenamine in addition to silver.

7. Conclusions

Argyria has been described in syphilitic patients in poor health who were therapeutically dosed with a total of about 1 g of silver in the form of silver arsphenamine together with other toxic metals. There have been no reports of argyria or other toxic effects resulting from the exposure of healthy persons to silver.

On the basis of present epidemiological and pharmacokinetic knowledge, a total lifetime oral intake of about 10 g of silver can be considered as the human NOAEL. As the contribution of drinking-water to this NOAEL will normally be negligible, the establishment of a health-based guideline value is not deemed necessary. On the other hand, special situations may exist where silver salts are used to maintain the bacteriological quality of drinking-water. Higher levels of silver, up to 0.1 mg/litre (a concentration that gives a total dose over 70 years of half the human NOAEL of 10 g), could then be tolerated without risk to health.

References


