WHO/SDE/WSH/03.04/14
English only

Silver in Drinking-water

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

Originally published in **Guidelines for drinking-water quality,** 2nd ed. Vol. 2. *Health criteria and other supporting information.* World Health Organization, Geneva, 1996.

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.

Acknowledgements

The work of the following coordinators was crucial in the development of this background document for development of WHO *Guidelines for drinking-water quality*:

J.K. Fawell, Water Research Centre, United Kingdom
(inorganic constituents)
U. Lund, Water Quality Institute, Denmark
(organic constituents and pesticides)
B. Mintz, Environmental Protection Agency, USA
(disinfectants and disinfectant by-products)

The WHO coordinators were as follows:

Headquarters:
H. Galal-Gorchev, International Programme on Chemical Safety
R. Helmer, Division of Environmental Health

Regional Office for Europe:
X. Bonnefoy, Environment and Health
O. Espinoza, Environment and Health

Ms Marla Sheffer of Ottawa, Canada, was responsible for the scientific editing of the document.

The efforts of all who helped in the preparation and finalization of this document, including those who drafted and peer reviewed drafts, are gratefully acknowledged.

The convening of the experts meetings was made possible by the financial support afforded to WHO by the Danish International Development Agency (DANIDA), Norwegian Agency for Development Cooperation (NORAD), the United Kingdom Overseas Development Administration (ODA) and the Water Services Association in the United Kingdom, the Swedish International Development Authority (SIDA), and the following sponsoring countries: Belgium, Canada, France, Italy, Japan, Netherlands, United Kingdom of Great Britain and Northern Ireland and United States of America.

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 ($AgNO_3$, CAS no. 7761-88-8) and silver chloride (AgCl, CAS no. 7783-90-6).

Physicochemical properties (1)

Property	*$AgNO_3$*	*AgCl*
Colour	White	White, darkens when exposed to light
Melting point (°C)	212	455
Water solubility at 25 °C (g/litre)	2150	0.00186

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*).

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*).

ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

Air

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

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 (*5*). 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.

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*).

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 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*).

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 deposed 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 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.

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

1. Holleman AF, Wiberg E. *Lehrbuch der anorganischen Chemie.* [*Textbook of inorganic chemistry.*] Berlin, Walter de Gruyter, 1985.
2. National Academy of Sciences. *Drinking water and health*. Washington, DC, 1977:289-292.
3. Whitlow SI, Rice DL. Silver complexation in river waters of central New York. *Water research*, 1985, 19:619-626.
4. Fowler BA, Nordberg GF. Silver. In: Friberg L, Nordberg GF, Vouk VB, eds. *Handbook on the toxicology of metals.* Amsterdam, Elsevier, 1986:521-531.
5. US Environmental Protection Agency. *Ambient water quality criteria for silver.* Washington, DC, 1980 (EPA 440/5-80-071).

6. Gibson RS, Scythes CA. Chromium, selenium and other trace element intake of a selected sample of Canadian premenopausal women. *Biological trace element research*, 1984, 6:105.
7. National Academy of Sciences. *Drinking water and health*, Vol. 4. Washington, DC, 1982.
8. Dequidt J, Vasseur P, Gromez-Potentier J. Étude toxicologique expérimentale de quelques dérivés argentiques. 1. Localisation et élimination. *Bulletin de la Société de Pharmacie de Lille*, 1974, 1:23-35 (cited in reference 5).
9. Nordberg GF, Gerhardsson L. Silver. In: Seiler HG, Sigel H, Sigel A, eds. *Handbook on the toxicity of inorganic compounds*. New York, NY, Marcel Dekker, 1988:619-624.
10. Furchner JE, Richmond CR, Drake GA. Comparative metabolism of radionuclides in mammals. IV. Retention of silver-110m in the mouse, rat, monkey, and dog. *Health physics*, 1968, 15:505-514.
11. Goldberg AA, Shapiro M, Wilder E. Antibacterial colloidal electrolytes: the potentiation of the activities of mercuric-, phenylmercuric- and silver ions by a colloidal sulphonic anion. *Journal of pharmacy and pharmacology*, 1950, 2:20-26.
12. Rungby J, Danscher G. Hypoactivity in silver exposed mice. *Acta pharmacologica et toxicologica*, 1984, 55:398-401.
13. Olcott CT. Experimental argyrosis. V. Hypertrophy of the left ventricle of the heart. *Archives of pathology*, 1950, 49:138-149.
14. Olcott CT. Experimental argyrosis. III. Pigmentation of the eyes of rats following ingestion of silver during long periods of time. *American journal of pathology*, 1947, 23:783-789.
15. Wagner PA, Hoekstra WG, Ganther HE. Alleviation of silver toxicity by selenite in the rat in relation to tissue glutathione peroxidase. *Proceedings of the Society of Experimental Biology and Medicine*, 1975, 148:1106-1110.
16. Nishioka H. Mutagenic activities of metal compounds in bacteria. *Mutation research*, 1975, 31:185-189.
17. Demerec M, Bertani G, Flint J. A survey of chemicals for mutagenic action on *E. coli*. *The American naturalist*, 1951, 85:119-136.
18. Denizeau F, Marion M. Genotoxic effects of heavy metals in rat hepatocytes. *Cell biology and toxicology*, 1989, 5:15-25.
19. Casto BC, Meyers J, DiPaolo JA. Enhancement of viral transformation for evaluation of the carcinogenic or mutagenic potential of inorganic salts. *Cancer research*, 1979, 39:193-198.
20. Furst A, Schlauder MC. Inactivity of two noble metals as carcinogens. *Journal of environmental pathology and toxicology*, 1977, 1:51-57.
21. Hill WR, Pillsbury DM. *Argyria, the pharmacology of silver*. Baltimore, MD, Williams and Wilkins, 1939 (cited in reference 5).
22. East BW et al. Silver retention, total body silver and tissue silver concentrations in argyria associated with exposure to an anti-smoking remedy containing silver acetate. *Clinical and experimental dermatology*, 1980, 5:305-311.
23. Westhofen M, Schäfer H. Generalized argyria in man: neurological, ultrastructural and X-ray microanalytic findings. *Archives of otorhinolaryngology*, 1986, 243:260-264.
24. Gaul LE, Staud AH. Clinical spectroscopy. Seventy cases of generalized argyrosis following organic and colloidal silver medication. *Journal of the American Medical Association*, 1935, 104:1387-1390.