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Iodine in Drinking-water

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

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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

CAS no.: 7553-56-2
Molecular formula: I_2

Physicochemical properties (*1,2*) [Also includes data from the Hazardous Substances Data Bank of the National Library of Medicine, Bethesda, MD] [Conversion factor in air: 1 ppm = 10 mg/m^3]

Property	*Value*
Boiling point	184.4 °C
Melting point	113.5 °C
Density	4.93 g/cm^3 at 25 °C
Vapour pressure	40 Pa at 25 °C
Water solubility	0.34 g/litre at 25 °C
Log octanol–water partition coefficient	2.49

Organoleptic properties

The taste and odour thresholds for iodine are 0.147–0.204 mg/litre in water and 9 mg/m^3 in air (*3*).

Major uses

Iodine is used as an antiseptic for skin wounds, as a disinfecting agent in hospitals and laboratories, and for the emergency disinfection of drinking-water in the field. Iodide is used in pharmaceuticals and in photographic developing materials.

Environmental fate

Iodine occurs naturally in water in the form of iodide (I^-), which is largely oxidized to iodine during water treatment.

ANALYTICAL METHODS

Iodide in water is normally determined by a titrimetric procedure which can be used for solutions containing 2–20 mg of iodide per litre. A leuco crystal violet method may be used for the determination of iodide or molecular iodine in water. This photometric method is applicable to iodide concentrations of 50–6000 µg/litre; the detection limit for iodine is 10 µg/litre (*4,5*).

ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

Water

The mean concentration of total iodine in drinking-water in the USA is 4 µg/litre, and the maximum concentration is 18 µg/litre (*2*). This is presumably predominantly iodide.

Food

The main natural sources of dietary iodide are seafood (200–1000 µg/kg) and seaweed (0.1–0.2% iodide by weight). Iodide is also found in cow's milk (20–70 µg/litre) and may be added to table salt (100 µg of potassium iodide per gram of sodium chloride) to ensure an adequate intake of iodine (*2,6*). The estimated dietary iodine requirement for adults ranges from 80 to 150 µg/day (*7*).

Estimated total exposure

Exposure to iodine may occur through drinking-water, pharmaceuticals, and food. At a concentration of 4 µg/litre in drinking-water, adult human daily intake will be 8 µg of iodine, on the assumption that 2 litres of drinking-water are consumed per day.

KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

Molecular iodine is rapidly converted into iodide following ingestion and this is efficiently absorbed throughout the gastrointestinal tract (*8*). Molecular iodine vapour is converted into iodide before absorption (*2*). The highest concentration of iodine in the human body is found in the thyroid, which contains 70–80% of the total iodine content (15–20 mg). Muscle and eyes also contain high iodide concentrations (*6,8*).

Iodine is an essential element in the synthesis of the thyroid hormones thyroxine (T_4) and triiodothyronine (T_3) through the precursor protein thyroglobulin and the action of the enzyme thyroid peroxidase. Iodide is excreted primarily by the kidneys and is partially reabsorbed from the tubules following glomerular filtration (*8*). Smaller amounts of iodine are excreted in saliva, sweat, bile, and milk (*9*).

EFFECTS ON LABORATORY ANIMALS AND *IN VITRO* TEST SYSTEMS

Acute exposure

The acute oral LD_{50} for potassium iodide in rats was 4340 mg/kg of body weight (3320 mg of iodide per kg of body weight), and the lowest oral lethal dose in mice was 1862 mg/kg of body weight (1425 mg of iodide per kg of body weight) (*9*).

Short-term exposure

The effects of iodide on autoimmune thyroiditis were investigated in two strains of chickens (CS and OS) known to be genetically susceptible to this disease. Administration of iodide in drinking-water (20 or 200 mg/litre, as potassium iodide) during the first 10 weeks of life increased the incidence of the disease, as determined by histological examination of the thyroid and measurement of T_3, T_4, and thyroglobulin antibodies. Excessive iodide consumption may increase the incidence of this disease in humans (*10*).

Reproductive toxicity, embryotoxicity, and teratogenicity

No effects were observed on ovulation rate, implantation rate, or fetal development in female rats given doses of 0, 500, 1000, 1500, or 2000 mg of iodide (as potassium iodide) per kg of diet during gestation and lactation. The dose-related survival rate for pups ranged from 93% (controls) to 16% (2000 mg/kg). Milk secretion was absent or greatly diminished in females exposed to iodide and the high mortality in pups was attributed to the dams' lactational failure (*11*).

The effects of iodide on brain enzymes in rat pups born to females given 1.1 mg of iodide per day as potassium iodide (about 37 mg/kg of body weight per day) in drinking-water were studied. Transient increases in glutamate dehydrogenase and decreases in succinate dehydrogenase were observed. Increases in phosphofructokinase and malate enzymes were noted, but no changes in hexokinase were reported. Serum T_4 levels did not differ significantly from control values (*12*).

Metabolism was severely disturbed in foals born to mares receiving excess iodine (48–432 mg of iodine per day) in the diet during pregnancy and lactation. The long bones of the legs of foals showed osteopetrosis (abnormally dense bones); phosphorus and alkaline phosphatase levels in the blood were elevated (*13*).

Carcinogenicity

In a study on the tumorigenic effects of iodide on the thyroid, groups of 20 rats were fed diets containing 0 or 1000 mg of iodide per kg as potassium iodide (0 or 39 mg of iodide per kg of body weight per day) for 19 weeks. No tumours were found on histopathological examination of the thyroid in either the treated or untreated groups (*14*). The exposure period may have been too short for a carcinogenic effect to be detected.

EFFECTS ON HUMANS

Short-term exposure

Oral doses of 2000–3000 mg of iodine (about 30–40 mg/kg of body weight) are estimated to be lethal to humans, but survival has been reported after ingestion of 10 000 mg. Doses of 30–250 ml of tincture of iodine (about 16–130 mg of total iodine per kg of body weight) have been reported to be fatal. Acute oral toxicity is primarily due to irritation of the gastrointestinal tract, marked fluid loss and shock occurring in severe cases. Exposure to iodine vapour results in lung, eye, and skin irritation, while high concentrations rapidly lead to pulmonary oedema (*2*).

In rare instances, a hypersensitization reaction may occur immediately after or within several hours of oral or dermal exposure to iodide. The most striking symptoms are angio-oedema (acute, transitory swelling of the face, hands, feet, or viscera) and swelling of the larynx, which may cause suffocation (*8*). Iodide has been used in the past as an expectorant in the treatment of asthma and related conditions at a typical dose of 3.3 mg/kg of body weight (*2*).

Long-term exposure

Chronic iodide exposure results in iodism; the symptoms resemble those of a sinus cold but may also include salivary gland swelling, gastrointestinal irritation, acneform skin, metallic or brassy taste, gingivitis, increased salivation, conjunctival irritation, and oedema of eyelids (*8*). Chronic ingestion of 2 mg of iodide per day (0.03 mg/kg of body weight per day) is considered by some authors to be excessive, but daily doses of 50–80 mg (0.8–1.3 mg/kg of body weight per day) are consumed by some Japanese without ill effect (*6*).

Chronic consumption of iodinated drinking-water has not been shown to cause adverse health effects in humans, although some changes in thyroid status have been observed. In a 5-year study of prison inmates consuming water containing iodine at a concentration of 1 mg/litre (approximately 0.03 mg/kg of body weight per day), no cases of hyper- or hypothyroidism, urticaria, or iodism were seen. However, a small but statistically significant decrease in radioactive iodine uptake by the thyroid and an increase in protein-bound iodine concentrations were reported (*15*). No adverse health effects were reported in men who drank

water providing iodide at doses of 0.17–0.27 mg/kg of body weight per day for 26 weeks (*16*).

In one study, the rate of radioactive iodide uptake by the thyroid was measured in 22 individuals with thyroid disease and 10 with normal thyroid function, before and after administration of 2.0 mg of iodide. Radioactive iodine uptake decreased by 54–99% in patients with thyroid disease but only by 8–54% in normal controls. These results suggest that iodide may aggravate certain pre-existing thyroid disease conditions (*17*).

Eight cases of congenital goitre and hypothyroidism in children were reported to be associated with maternal ingestion of iodide (*18*). Estimates of maternal iodide exposure ranged from 12 to 1650 mg/day (about 0.02–27 mg/kg of body weight per day) in individuals taking iodide as an expectorant in the treatment of asthma. No direct evidence of a cause-and-effect relationship between iodide exposure and health effects during pregnancy was reported.

Hypothyroidism has also been reported in infants of mothers receiving multiple topical applications of povidone–iodine (about 1% free iodine) during pregnancy and lactation (*19*).

CONCLUSIONS

In 1988, JECFA set a PMTDI for iodine of 1 mg/day (17 µg/kg of body weight per day) from all sources, based mainly on data on the effects of iodide (*20*). However, recent data from studies in rats indicate that the effects of iodine in drinking-water on thyroid hormone concentrations in the blood differ from those of iodide (*21,22*).

Available data therefore suggest that derivation of a guideline value for iodine on the basis of information on effects of iodide is inappropriate, and there are few relevant data on the effects of iodine. Because iodine is not recommended for long-term disinfection, lifetime exposure to iodine from water disinfection is unlikely. For these reasons, a guideline value for iodine has not been established at this time.

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