
Chromium

A maximum acceptable concentration of 0.05 mg/L ($50 \text{ }\mu\text{g/L}$) for chromium in drinking water has been established on the basis of health considerations. Trivalent chromium, the most common naturally occurring state of chromium, is not considered to be toxic; however, if present in raw water, it may be oxidized to hexavalent chromium during chlorination. Toxic effects of chromium in man are attributed primarily to this hexavalent form. At the maximum acceptable concentration in drinking water, ingestion of hexavalent chromium has not resulted in any known harmful effects on the health of man or animals.

General

Chromium can exist in valences from -2 to 6 but is present in the environment mainly in the trivalent or hexavalent state. Trivalent chromium (Cr[III]) is the most common naturally occurring state; most soils and rocks contain small amounts of chromic oxide (Cr_2O_3). Hexavalent chromium (Cr[VI]) occurs infrequently in nature, and chromates (CrO_4^{2-}) and dichromates ($\text{Cr}_2\text{O}_7^{2-}$) present in the environment are generally the result of industrial and domestic emissions. Chromium is present in Canadian soils at concentrations ranging from 20 to 125 $\text{mg/kg}^{(1)}$ and is found in trace quantities in most plant and animal tissues.

Chromium is widely used in industry. The hexavalent chromium compounds are used in the metallurgical industry for chrome alloy and chromium metal production and chrome plating, and in the chemical industry as oxidizing agents and in the production of other chromium compounds. Trivalent chromium salts are used less widely, being employed in textile dyeing, in the ceramic and glass industry, and in photography.

The only commercially important chromium mineral is chromite (FeOCr_2O_3). Canadian deposits of this mineral are usually low-grade, and consequently all Canadian requirements for chromium are filled by importation. Canadian consumption of chromite in 1981 was 24 771 tonnes.⁽²⁾

Occurrence

Of the common trivalent chromium salts, the chloride, nitrate, and sulphate are readily soluble in water; the hydroxide and carbonate are quite insoluble. Of the common hexavalent chromium salts, only sodium, potassium, and ammonium chromates and the corresponding dichromates are soluble. Most of the chromium in soils is present in the form of highly insoluble chromites. Weathering, oxidation, and bacterial action convert these chromites into soluble forms, and in this way chromium mineral deposits contribute slightly to the chromium content of natural waters. Chromium can also be present in natural waters as a contaminant from the discharge of industrial wastes or water from cooling systems in which chromates are used as corrosion inhibitors.

Total dissolved chromium is the parameter most often determined in trace element analyses of surface and ground waters. It is generally assumed that the trivalent form is not likely to be present in waters of pH 5 or above because of the low solubility of the hydrated oxide.⁽³⁾ In preliminary studies, both trivalent and hexavalent forms have been shown to exist in surface waters. Analysis of samples from the Upper Susquehanna River Basin in New York State revealed the predominance of chromium(III) in uncontaminated waters and an increase in the mean chromium(VI) content of the river downstream from a sewage outfall.⁽⁴⁾ Chromium(III) added to natural lake waters is converted very slowly to chromium(VI).⁽⁵⁾ In chlorinated drinking water, chromium is usually present in the hexavalent state.

Chromium is generally present at low concentrations in Canadian surface waters. Concentrations in the Great Lakes averaged approximately 0.001 mg/L (range 0.0002 to 0.019 mg/L),^(6,7) and concentrations in Canadian rivers were between 0.002 and 0.023 mg/L .⁽⁷⁾ Data from NAQUADAT stations during the period 1980 to 1985 showed that, for the Central region of Canada, total chromium concentrations in raw water ranged from the detection limit of 0.002 mg/L to 0.044 mg/L ; for the Atlantic region, the concentrations ranged from the same

detection limit to 0.024 mg/L.⁽⁸⁾ Concentrations of chromium in Canadian waters have been stated to be usually less than 0.025 mg/L.⁽¹⁾

A survey of Canadian drinking water supplies suggested that the maximum concentrations of chromium in raw water and in treated and distributed waters were 0.014 and 0.009 mg/L, respectively. The median concentration of chromium in three types of water was 0.002 mg/L.⁽⁹⁾ Chromium concentrations above 0.001 mg/L were detected in only 11 percent of samples taken at consumers' taps from 969 U.S. water systems; the average concentration of chromium in these samples was 0.0023 mg/L.⁽¹⁰⁾

There is insufficient information to indicate mean concentrations of chromium in the air of Canadian communities. The concentrations of chromium in air samples from five remote areas in Canada ranged from 0.0000032 to 0.000025 mg/m³.⁽¹¹⁾ In the United States, chromium concentrations in urban air ranged from less than 0.00001 mg/m³ to 0.00005 mg/m³.⁽¹²⁾

Foods vary considerably in chromium content. Milk and dairy products (mean, 0.06 mg/kg), meat (0.07 mg/kg), cereal (0.17 mg/kg), potatoes (0.05 mg/kg), fruits (0.06 mg/kg), and sugars (0.34 mg/kg) are the main dietary sources of this element.⁽¹³⁾ Concentrations of chromium ranging from 0.13 to 0.85 mg/kg have been recorded in a variety of seafoods commercially available in Canada.⁽¹⁴⁾ Carbonated beverages and fruit juices generally contain less than 0.01 mg/L.⁽¹⁵⁾ Chromium concentrations in imported and domestic wines available in Canada were between 0.02 and 0.06 mg/L.⁽¹⁶⁾ Chromium occurs in food mainly in the trivalent form, although as much as 63 percent of the total chromium in some foods is present in the hexavalent form.⁽¹⁷⁾ In cooked food, levels of chromium may be slightly higher because of the contribution from stainless steel utensils.

Canadian Exposure

Recent analyses of self-selected Canadian diets (including drinking water) found the mean dietary intake of chromium to be approximately 0.055 mg/day, with a range of approximately 0.01 to 0.16 mg/day.⁽¹⁸⁾ Studies in the United States have estimated the mean daily intake to be 0.06 to 0.09 mg.^(19,20) All these values are significantly lower than earlier estimates of approximately 0.2 mg/day,^(13,21) possibly as a result of improvements in analytical techniques.^(18,22)

Assuming daily water consumption to be 1.5 L⁽²³⁾ and the average chromium concentration of Canadian drinking water to be 0.002 mg/L, the average daily intake of chromium from drinking water would be 0.003 mg per person. This value compares well with U.S. estimates of 0.004 to 0.005 mg.^(11,24) Chromium intake from food is substantially higher than that from

drinking water; the mean total daily intake of chromium from water would be roughly 10 percent of the total dietary intake estimated above.

If the concentration of chromium in air in Canada is assumed to be 0.000015 mg/m³⁽²⁵⁾ and an individual's daily respiratory volume to be 20 m³, then the daily intake of chromium from air would be 0.0003 mg. One U.S. estimate of the daily intake of chromium from air is 0.00028 mg.⁽²⁴⁾ The U.S. National Academy of Sciences has estimated this quantity to be only 0.00004 to 0.00008 mg.⁽²⁶⁾ Chromium is also present in cigarettes.⁽²⁷⁾

Based on the above considerations, the total daily intake of chromium from food, air, and water would be about 0.06 mg. Intake for smokers may be higher because of the presence of chromium in cigarettes.

Treatment Technology

Because chromium has not been identified as a problem in many water supplies, there have been few studies to determine the effectiveness of water treatment processes in removing chromium. Most of the information is based on laboratory or pilot-plant studies.⁽²⁸⁾

Of the two common valence states of chromium, chromium(III) is the less toxic and the easier to remove from water supplies. Alum coagulation, iron coagulation (using ferric sulphate), and lime softening have all been found to be capable of removing at least 90 percent of an initial chromium(III) concentration of 0.15 mg/L. The effectiveness of iron coagulation was independent of pH in the range of 6.5 to 9.3. Alum coagulation was most effective between pH 7.5 and 8.5 and removed only about 80 percent of the chromium at pH 9.2. The optimum range for lime softening was above pH 10.5; the amount of chromium removed decreased to about 70 to 80 percent at pH 9.5. At an initial chromium concentration of 10 mg/L, all three processes were capable of reducing the chromium concentration by 98 percent.⁽²⁹⁾

None of these three methods is very effective in removing hexavalent chromium. The best results were found using iron coagulation with ferric sulphate, which removed 35 percent of the hexavalent chromium at pH 5.5. Neither alum coagulation nor lime softening removed more than 10 percent.⁽²⁹⁾

The method of choice for removing hexavalent chromium is iron coagulation using ferrous sulphate, which reduces the chromium to the trivalent state. Studies on river water containing 0.15 mg/L of chromium(VI) showed that ferrous sulphate was capable of removing 98 percent of the chromium in the pH range 6.5 to 9.3. For initial chromium(VI) concentrations above about 0.2 mg/L, it was found necessary to adjust the pH several minutes after coagulation to allow time for the chromium(VI) to be reduced to chromium(III).⁽²⁹⁾

Chlorination of water before treatment tends to oxidize any trivalent chromium to the hexavalent state and so reduce the effectiveness of water treatments aimed at chromium(III). Chlorine doses of 2 mg/L with contact times of up to 6 hours decreased the effectiveness of alum coagulation by only about 10 percent, but much larger decreases were found with longer contact times.⁽²⁹⁾ Chlorination of water after treatment would be expected to convert any residual trivalent chromium to the hexavalent state. It is not clear, however, if passage of water through iron pipes would tend to reverse the process.

Health Considerations

Essentiality

Only the trivalent and hexavalent forms of chromium appear to be of significance in biological systems,⁽³⁰⁾ and only the trivalent form appears to be essential.⁽³¹⁾ Trivalent chromium is necessary for the synthesis of fat from glucose and also for the oxidation of fat to carbon dioxide. The biologically active form of the element is believed to be a nicotinic acid – amino acid (glycine, glutamic acid, and cysteine) – trivalent chromium complex, which functions as a potentiator of insulin, possibly by forming a complex between sulfhydryl groups on the cell membrane and sulfhydryl groups on the A chain of insulin.^(32,33) This complex, which occurs in a variety of foods, is termed glucose tolerance factor (GTF). The primary biochemical effect from chromium deficiency is decreased sensitivity to exogenous or endogenous insulin.⁽³³⁾

There is increasing evidence that chromium deficiency may also be a basic factor in atherosclerosis.^(34,35) In animals, severe deficiency results in decreased growth rates and life spans, increased concentrations of serum cholesterol, and increased formation of aortic plaques. Under certain conditions, a syndrome resembling diabetes mellitus, with fasting hyperglycaemia and glycosuria, has been produced. Low levels of chromium in plasma or hair have also been correlated with increased likelihood of coronary artery disease.^(36,37) The U.S. Food and Nutrition Board has set an adequate and safe range for chromium intake at 0.05 to 0.2 mg/day.⁽³⁸⁾

Absorption, Distribution, and Excretion

Estimates of the fraction of chromium that is absorbed by the intestine vary. It has been reported that about 2 to 10 percent of the hexavalent chromium ingested is absorbed, as is 0.1 to 3 percent of the inorganic trivalent chromium.^(39,40) Absorption of 2.1 percent of ingested chromium(VI) has been estimated in humans.⁽⁴¹⁾ From studies on rats, it has been estimated that the fraction of chromium(VI)

absorbed is nine times greater than that of chromium(III).⁽⁴²⁾ Other estimates put the absorption of both inorganic chromium species in the range of 0.5 to 3 percent.^(43,44) Gastric juice inhibits absorption of both trivalent and hexavalent inorganic chromium and partially reduces the hexavalent form to the trivalent.⁽⁴¹⁾ Chromium is much more readily absorbed in the GTF (organic) form than in the inorganic form. At least 10 to 25 percent of ingested organic chromium is thought to be absorbed from the intestinal tract, probably the jejunum or upper ileum.^(18,34,39) Intestinal chromium absorption in young children proceeds at a greater rate than that in adults.⁽⁴⁵⁾ Because the proportion of ingested chromium that is hexavalent, trivalent, inorganic, or organically bound is unknown, the amount of chromium absorbed per day cannot be reliably estimated. For example, a document published by the World Health Organization estimates that 10 percent of the chromium ingested is absorbed,^(40,46) which implies that the mean daily uptake of chromium from a Canadian diet is about 0.006 mg. However, an independent estimate of the U.S. daily uptake is 0.001 mg or less.⁽²³⁾

Airborne chromium-containing particles with mass greater than 0.001 mg are believed not to reach the alveoli at all, but to be trapped in the bronchi. These particles are later moved to the pharynx by ciliary action and swallowed. This route of exposure could therefore contribute to dietary intake.⁽⁴⁷⁾ A portion of inhaled chromium-containing aerosols deposits in the respiratory tract. Insoluble particles small enough to penetrate the alveoli may be trapped in the tissue. If the particles can be dissolved, chromium may enter the blood and be distributed throughout the body.

The metabolism of ingested chromium depends on its chemical form. Chromium chloride administered parenterally to rats disappears rapidly from the bloodstream and is most strongly absorbed by the ovaries or testes and spleen, whereas chromium administered as the organic complex, GTF, accumulates mainly in the liver. The fate of inhaled trivalent chromium differs from that of the hexavalent form. Thirty days after intratracheal injection of chromium-containing aerosol to guinea pigs, 30 percent of the trivalent chromium, but only 2.4 percent of the hexavalent chromium, remained in the lung tissue.⁽⁴⁸⁾ The concentration of chromium in red blood cells, liver, kidney, and spleen was greater following intratracheal administration of hexavalent chromium.

In studies using rodents, it has been shown that chromium can cross the placenta. Estimates of the fraction of the dose of inorganic chromium transferred to the foetus were 0 to 12 percent for chromium(VI) and 0.4 percent for chromium(III).⁽⁴⁹⁾ In contrast, 20 to

50 percent of chromium administered in the form of GTF was found in the litters.⁽⁵⁰⁾ This is consistent with the role of chromium as an essential trace element.⁽⁴³⁾

There seems to be a homeostatic mechanism involving hepatic or intestinal transport systems that prevents excessive accumulation of trivalent chromium.⁽⁵¹⁾ In man, the largest stores of chromium are in skin, muscle, and fat; the highest concentration is in the lungs. The average total chromium content of the body is approximately 6 mg,⁽¹⁸⁾ but tissue levels vary according to the sex, age, and geographical location of the individual.⁽³⁴⁾

At least 80 percent of excreted chromium is eliminated in the urine; the remainder is eliminated in the faeces. There is little agreement on the amount of daily urinary chromium excretion. A mean 24-hour excretion value of 0.0084 mg with a range of 0.002 to 0.021 mg is believed to be representative, although a recent estimate places the mean at less than 0.001 mg.⁽²³⁾ Very high chromium excretion appears to occur in some insulin-dependent diabetics. Absorbed chromium is eliminated from the body in a rapid phase (1 to 2 days) representing clearance from the blood, and in a slower phase representing clearance from tissues. Adipose and muscle tissues retain chromium for about two weeks, whereas the liver and spleen may store chromium for as long as 12 months.⁽⁴³⁾

Toxic Effects

The known harmful effects of chromium in man are attributed primarily to the hexavalent form; trivalent chromium is considered non-toxic. A single oral dose of 10 mg/kg body weight of hexavalent chromium will result in liver necrosis, nephritis, and death in man. A lesser dose will cause irritation and corrosion of the gastrointestinal mucosa and occasionally encephalitis and enlarged liver. No local or systemic effects have been attributed to the ingestion of trivalent chromium.

Consumption of drinking water with a hexavalent concentration of 1 to 25 mg/L for 3 years caused no ill effects in a family of four.⁽⁵²⁾

Ingestion of drinking water containing 25 mg of hexavalent chromium (potassium chromate) per litre resulted in an eightfold increase in tissue chromium concentration over that found in rats that had consumed trivalent chromium (chromic chloride) at 25 mg/L for the same six-month period.⁽⁵³⁾ Toxic effects have been observed in rats and rabbits following ingestion of drinking water with a hexavalent chromium concentration above 5 mg/L, but ingestion of water containing 11.2 mg/L for 4 years caused no ill effects in dogs. Drinking water with a chromium concentration of 25 mg/L administered to rats for six months caused no deleterious effects.⁽³⁰⁾

Inhalation of air containing high concentrations of chromium causes respiratory damage and cancer (see below).

Carcinogenicity

Hexavalent chromium can inhibit benzpyrene hydroxylase activity. It has been suggested that compounds capable of such inhibition are carcinogenic.⁽⁵⁴⁾

In humans, exposure to hexavalent chromium salts for periods of 2 to 26 years has been implicated as a cause of cancer of the digestive tract. High levels of chromium (and zinc) in soil have been correlated with regional incidences of stomach cancer.⁽⁵⁵⁾ Lead chromate is believed to have caused the deaths, from cancer, of five occupationally exposed individuals.⁽⁵⁶⁾ Based on exposure to chromium via inhalation, the International Agency for Research on Cancer has categorized "chromium and certain chromium compounds" in Group 1: sufficient evidence for carcinogenicity in humans and animals.⁽⁵⁷⁾ However, a recent report by the U.S. Environmental Protection Agency states that there are inadequate data to conclude that chromium is carcinogenic via ingestion.⁽³⁹⁾

Mutagenicity

Hexavalent chromium is mostly inactive on isolated nuclei and purified DNA but is able to induce every kind of genetic effect in intact cells and whole mammals, whereas trivalent chromium shows the opposite tendency. This behaviour is attributed to the fact that trivalent chromium usually crosses cell membranes only slowly and is therefore unlikely to reach the nucleus of intact cells. In contrast, hexavalent chromium crosses cell membranes readily, in part by active transport; once inside the cell, it is partially reduced to the trivalent state, which produces genotoxic effects.⁽⁵⁸⁾ Once inside the cell, trivalent chromium can form tight complexes with DNA, accounting for its mutagenic potential.⁽⁵⁹⁾ Compounds of both trivalent and hexavalent chromium increase non-complementary nucleotide incorporation into DNA, with hexavalent chromium being effective at lower doses.^(50,60) Exposure of cells from rat liver and kidney to hexavalent chromium leads to increased cross-linking in DNA.⁽³⁹⁾ Positive Ames tests have been reported for hexavalent chromium but not for trivalent chromium.^(61,62)

Teratogenic and Reproductive Effects

There is no evidence that chromium compounds have produced birth defects or reproductive deficits in man.⁽⁴³⁾ Animal studies have attributed malformations such as cleft palate and skeletal defects to chromium, but the effects may have been the secondary result of maternal toxicity.⁽⁴³⁾

Rationale

1. Trivalent chromium (Cr(III)) is the most common natural state of chromium and is essential in man and animals for efficient lipid, glucose, and protein metabolism. Chromium(III) is considered non-toxic; however, if present in raw water, it is oxidized to hexavalent chromium (Cr(VI)) during chlorination. Chromium(VI) is not considered an essential nutrient, and known harmful effects of chromium in man are attributed primarily to this form.

2. Knowledge of the toxic effects of hexavalent chromium is derived almost entirely from occupational exposures, with the main effects being observed on the skin and respiratory tract. At the present maximum acceptable concentration in drinking water (0.05 mg/L), hexavalent chromium has not had any known harmful effects on the health of man or animals. Data available are insufficient to determine whether higher concentrations would be equally safe.

3. The maximum acceptable concentration for chromium in drinking water is therefore 0.05 mg/L. Available survey data indicate that concentrations of total chromium in drinking water are low, averaging 0.0023 mg/L. Although chromium salts impart odour and taste to water, the concentration at which this occurs, 1.5 mg/L, is considerably higher than the maximum acceptable concentration.

References

- National Research Council of Canada. Effects of chromium in the Canadian environment. NRCC No. 15017, Associate Committee on Scientific Criteria for Environmental Quality, Ottawa (1976).
- Law-West, D.G. Chromium. In: Canadian minerals yearbook 1982. Mineral Report No. 32, Mineral Resources Branch, Energy, Mines and Resources Canada, Ottawa (1984).
- National Academy of Sciences/National Academy of Engineering. Water quality criteria. Committee on Water Quality Criteria, Washington, DC (1972).
- Pankow, J.F. *et al.* Analysis for chromium traces in the aquatic ecosystem. II. A study of Cr(III) and Cr(VI) in the Susquehanna River Basin of New York and Pennsylvania. *Sci. Total Environ.*, 7: 17 (1977).
- Schroeder, D.C. and Lee, G.F. Potential transformations of chromium in natural waters. *Water Air Soil Pollut.*, 4: 355 (1975).
- Weiler, R.R. and Chawla, V.K. Dissolved mineral quality of Great Lakes waters. In: Proc. 12th Conf. on Great Lakes Research. p. 801 (1969).
- Durum, W.H. and Haffty, J. Occurrence of minor elements in water. *U.S. Geol. Surv. Circ. No. 445* (1961).
- National Water Quality Data Bank (NAQUADAT). Water Quality Branch, Inland Waters Directorate, Environment Canada, Ottawa (1985).
- Méranger, J.C., Subramanian, K.S. and Chalifoux, C. A national survey of cadmium, chromium, copper, lead, zinc, calcium, and magnesium in Canadian drinking water supplies. *Environ. Sci. Technol.*, 13(6): 707 (1979), cited in reference 28.
- Craun, G.F. and McCabe, L.J. Problems associated with metals in drinking water. *J. Am. Water Works Assoc.*, 67: 593 (1975).
- Rahn, K.A. Sources of trace elements in aerosols — an approach to clean air. Technical report, Department of Meteorology and Oceanography, University of Michigan, Ann Arbor, MI (1971), cited in reference 1.
- Norseth, T. The carcinogenicity of chromium. *Environ. Health Perspect.*, 40: 121 (1981).
- Kirkpatrick, D.C. and Coffin, D.C. The trace metal content of representative Canadian diets in 1970 and 1971. *Can. Inst. Food Sci. Technol. J.*, 7: 56 (1974).
- Méranger, J.C. and Somers, E. Determination of the heavy metal content of sea-foods by atomic-absorption spectrophotometry. *Bull. Environ. Contam. Toxicol.*, 3: 360 (1968).
- Méranger, J.C. The heavy metal content of fruit juices and carbonated beverages by atomic absorption. *Bull. Environ. Contam. Toxicol.*, 5: 271 (1970).
- Méranger, J.C. and Somers, E. Determination of heavy metals in wine by atomic absorption spectrophotometry. *J. Assoc. Off. Anal. Chem.*, 51: 4 (1968).
- Schroeder, H.A. The role of chromium in mammalian nutrition. *Am. J. Clin. Nutr.*, 21: 230 (1968).
- Gibson, R.S. and Scythes, C.A. Chromium, selenium, and other trace element intakes of a selected sample of Canadian premenopausal women. *Biol. Trace Elem. Res.*, 6: 105 (1984).
- Hammond, P.B. and Beliles, R.P. Metals in toxicology. In: The basic science of poisons. 2nd edition. J. Doull, C.D. Klassen and M.O. Amdur (eds.). Macmillan, New York, NY. p. 409 (1980), cited in reference 43.
- Kumpulainen, J.T., Wolf, W.R., Veillon, C. and Mertz, W. Determination of chromium in selected United States diets. *J. Agric. Food Chem.*, 27: 490 (1979), cited in reference 43.
- Méranger, J.C. and Smith, D.C. The heavy metal content of a typical Canadian diet. *Can. J. Public Health*, 63: 53 (1972).
- Borel, J.S. and Anderson, R.A. Chromium. In: Biochemistry of the essential ultratrace elements. E. Frieden (ed.). Plenum Press, New York, NY. p. 175 (1984).
- Armstrong, V.C., Holliday, M.G. and Schrecker, T.F. Tap water consumption in Canada. Environmental Health Directorate Report 82-EHD-80, Department of National Health and Welfare, Ottawa (1981).
- Schroeder, H.A. Chromium air quality. Monograph No. 70-15, American Petroleum Institute, Washington, DC (1970).
- U.S. Public Health Service/National Air Pollution Control Administration. Preliminary air pollution survey of chromium and its compounds. A literature review. National Bureau of Standards, Clearinghouse of Federal Scientific and Technical Information, U.S. Department of Commerce, Springfield, VA (1969).
- National Academy of Sciences. Chromium. Committee on Biological Effects of Atmospheric Pollutants, Washington, DC (1974).
- Cogbill, E.C. and Hobbs, M.E. Transfer of metallic constituents of cigarettes to the main-stream smoke. *Tobacco Sci.*, 144: 68 (1957).
- McDonald, R.A. Water treatment technology review: control of chemical contaminants. Prepared for the Department of National Health and Welfare by M.R.2 — McDonald & Associates (Draft) (1985).

29. U.S. Environmental Protection Agency. Manual of treatment techniques for meeting interim primary drinking water regulations. Document EPA-600/8-77-005, Municipal Environment Research Laboratory, Water Supply Research Division, Office of Research and Development, Cincinnati, OH (1977).
30. Mertz, W. Chromium occurrence and function in biological systems. *Physiol. Rev.*, 49: 163 (1969).
31. Levander, O.A. Selenium and chromium in human nutrition. *J. Am. Diet. Assoc.*, 66: 338 (1975).
32. Mertz, W. Chromium and its relation to carbohydrate metabolism. *Med. Clin. North Am.*, 60: 739 (1976).
33. Mertz, W. Newer essential trace elements, chromium, tin, vanadium, nickel and silicon. *Proc. Nutr. Soc.*, 33: 307 (1974).
34. Schroeder, H.A., Nason, A.P. and Tipton, I.H. Chromium deficiency as a factor in atherosclerosis. *J. Chronic Dis.*, 23: 123 (1970).
35. Mautner, G. and Dinoeua, S. The content of hexavalent chromium in water sources and its effect on the development of experimental atherosclerosis in warm blooded animals. *Gig. Sanit.*, 39: 78 (1974).
36. Simonoff, M. *et al.* Low plasma chromium in patients with coronary artery and heart diseases. *Biol. Trace Elem. Res.*, 6: 431 (1984).
37. Cote, M. *et al.* Hair chromium concentration and coronary artery disease in Canada, France, Spain and Italy. *Nutr. Res., Suppl. I*: 356 (1985).
38. U.S. Food and Nutrition Board. Recommended daily allowances. 9th rev. edition. National Academy of Sciences, Washington, DC (1980), cited in reference 18.
39. U.S. Environmental Protection Agency. Chromium: health advisory. Office of Drinking Water (Draft) (1985).
40. World Health Organization. Guidelines for drinking water quality. Vol. 2: Health criteria and other supporting information. Ch. 6. Geneva (1984).
41. Donaldson, R.M., Jr. and Barreras, R.F. Intestinal absorption of trace quantities of chromium. *J. Lab. Clin. Med.*, 68: 484 (1966), cited in reference 39.
42. MacKenzie, R.D. *et al.* Chronic toxicity studies. II. Hexavalent and trivalent chromium administered in drinking water to rats. *Arch. Ind. Health*, 18: 232 (1958), cited in reference 40.
43. O'Heany, J.M. Summary of health effects of chromium. Health Studies Service, Special Studies and Services Branch, Ontario Ministry of Labour (1986).
44. Underwood, E.J. Trace elements in human and animal nutrition. 4th edition. Academic Press, New York, NY. pp. 258–270 (1977), cited in reference 43.
45. Saner, G. and Gunson, C.T. Hair chromium concentration in newborns and their mothers. *Nutr. Rep. Int.*, 14: 155 (1976).
46. Friberg L. *et al.* Chromium. In: Handbook on the toxicology of metals. Elsevier/North-Holland Biomedical Press, Amsterdam (1979), cited in reference 40.
47. Natusch, D.F.S. and Wallace, J.R. Urban aerosol toxicity: the effect of particle size. *Science*, 186: 695 (1974).
48. Baetjer, A.M., Damron, C. and Budacz, V. The distribution and retention of Cr in men and animals. *Arch. Ind. Health*, 20: 54 (1959), cited in reference 1.
49. Danielsson, B.R.G., Hassoun, E. and Dencker, L. Embryotoxicity of chromium: distribution in pregnant mice and effects on embryonic cells *in vitro*. *Arch. Toxicol.*, 51: 233 (1982), cited in reference 43.
50. Majone, F. and Rensi, D. Mitotic alterations, chromosome aberrations and sister chromatid exchanges induced by hexavalent and trivalent chromium on mammalian cells *in vitro*. *Caryologia*, 32: 379 (1979), cited in reference 39.
51. Schroeder, H.A., Balassa, J.J. and Tippon, I.H. Abnormal trace metals in man: chromium. *J. Chronic Dis.*, 15: 941 (1962).
52. Davids, H.W. and Lieber, M. Underground water contamination by chromium wastes. *Water Sewage Works*, 98: 528 (1951).
53. Byerrum, R.V. Some studies on the chronic toxicity of cadmium and hexavalent chromium in drinking water. *Perdue Univ. Eng. Ext. Ser.*, 106: 1 (1961).
54. Chretien, J. and Thieblemont, M. Un mécanisme intermédiaire dans la carcinogénèse pulmonaire. *Nouv. Presse Med.*, 3: 1347 (1974).
55. Stocks, P. N.B.E.C.C. Annu. Rep., 35: 95 (1957). Cited in Williams, D.R. Metals, ligands, and cancer. *Chem. Rev.*, 72: 203 (1972).
56. Finklea, J.F. Lead chromate — an update. Letter dated October 8, 1976, from U.S. Department of Health, Education and Welfare/National Institute for Occupational Safety and Health.
57. International Agency for Research on Cancer. IARC Monogr. Eval. Carcinog. Risk Chem. Man, Suppl. 4: 91 (1982).
58. Bianchi, V. and Levis, A.G. Mechanisms of chromium genotoxicity. In: Carcinogenic and mutagenic metal compounds. E. Merian *et al.* (eds.). Gordon and Breach Science Publ., London, UK. pp. 269–293 (1985).
59. U.S. Environmental Protection Agency. Health effects criteria document for chromium. Criteria and Standards Division, Office of Drinking Water, Washington, DC (1985), cited in reference 39.
60. Raffetto, G. *et al.* Direct interaction with cellular targets as the mechanism for chromium carcinogenesis. *Tumori*, 63: 503 (1977), cited in reference 39.
61. Petrilli, F.L. and De Flora, S. Oxidation of inactive trivalent chromium to the mutagenic hexavalent form. *Mutat. Res.*, 58: 167 (1978), cited in reference 39.
62. Gentile, J.M., Hyde, K. and Schubert, J. Chromium genotoxicity as influenced by complexation and rate effects. *Toxicol. Lett.*, 7: 439 (1981), cited in reference 39.