Tantalum

(CAS No: 7440-25-7)

Health-based Reassessment of Administrative Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

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1 Introduction

The present document contains the assessment of the health hazard of tantalum by the Committee on Updating of Occupational Exposure Limits, a committee of the Health Council of the Netherlands. The first draft of this document was prepared by AAE Wibowo, Ph.D. (Coronel Institute, Academic Medical Centre, Amsterdam, the Netherlands).

The evaluation of the toxicity of tantalum has been based on the reviews by the American Conference of Governmental Industrial Hygienists (ACGIH) (ACG98) and by Goering and Fowler (Goe91). Where relevant, the original publications were reviewed and evaluated as will be indicated in the text. In addition, in March 1998, literature was searched in the databases Medline, Embase, and Chemical Abstracts, starting from 1966, 1988, and 1970, respectively, and using the following key words: tantalum, TA, and 7440-25-7. HSELINE, NIOSHTIC, CISDOC, MHIDAS (covering the period 1985/1987 until 1998), and POLTOX (Toxline, Cambridge Sc Abstr, and FSTA; covering the period 1990 until 1995), databases available from CD-ROM, were consulted as well.

In July 2000, the President of the Health Council released a draft of the document for public review. No comments were received.

An additional search in Toxline and Medline in November 2003 did not result in information changing the committee's conclusions.

2 Identity

name	:	tantalum
synonyms	:	-
molecular formula	:	Ta
CAS number	:	7440-25-7

3 Physical and chemical properties

atomic weight	:	180.95
boiling point	:	5429°C
melting point	:	2996°C
flash point	:	-
vapour pressure	:	-
solubility in water	:	insoluble
log $P_{octanol/water}$	:	0.23 (estimated)
conversion factors	:	not applicable

Data from ACG98, NLM03, http://esc.syrres.com.

Tantalum occurs as a black powder or steel-blue or, if polished, platinum-white metal sheets or bars. Tantalum has high resistance to corrosion from acids, alkalis, mine and sea water, sulphur dioxide, and chlorine solutions (ACG98).

4 Uses

Tantalum metal is used in electric capacitors, chemical equipment, rectifiers, furnace components, high-speed tools, body implants, and electronic circuitry. The oxide of tantalum is employed in making optical glass and has piezoelectric, maser, and laser applications (ACG98).

5 Biotransformation and kinetics

Sill et al. reported on a case of accidental inhalation exposure to 30 Cu of ^{182}Ta and 150 Cu of ^{183}Ta at a nuclear reactor test site. Within 7 days, 93% of the radioactivity was eliminated entirely through the faeces. The remaining radioactivity was slowly eliminated at a rate of 0.05% per day. No radioactivity was detected in the 24-hour urine (Sil69). Edel et al. presented results of clinical examinations of a case of hard metal pneumoconiosis in a patient, who had worked for 13 years as a grinder cutting hard metals, performed 3 years after having stopped work. Analysis of metals in the lung tissue showed abnormal concentrations of tungsten (107 ppm), tantalum (32.5 ppm), and cobalt (2.4 ppm). The tantalum concentrations in broncheolar lavage and in blood were 10,000-fold or more higher than those in control subjects. There was no significant urinary tantalum excretion (Ede86). Subsequent *in vitro* studies with human plasma and lung components showed that the highest concentrations of

the 3 elements were found in the soluble fraction of cytoplasma. Tantalum in plasma was strongly bound to proteins, whereas in the lung cytosol, it was distributed among the macromolecules and the high molecular and low molecular fractions. However, when the tantalum-containing lung cytosol was incubated with pure human plasma, the highest amount of tantalum was strongly bound to proteins suggesting that plasma would be able to mobilise tantalum from the lungs, even when associated to higher molecular weight components of the pulmonary cytoplasmic fractions. Edel et al. suggested that this could explain the still high tantalum blood concentration in the worker 3 years after the end of exposure (Ede86, Ede90).

Gamsu et al. studied the pulmonary clearance of tantalum powder in 26 patients by radiographic method. The mean mass diameter of the tantalum particles was 2.4 μm, and the quantity of tantalum used varied from 0.5 to 1.0 mL. Serial radiographs were obtained up to 15 months after tantalum insufflations. In 8 patients, the clearance was complete within 20 hours. In 18 patients, the clearance showed an orderly progression from large to small airways, except for distal bronchioles, which disclosed no clearance for the first 24 to 48 hours. In the terminal units, radiopacity usually increased during the first 10 to 48 hours, and no significant clearance occurred up to 15 months (Gam73).

The committee found a few animal studies on the kinetics of tantalum dusts. Long-term retention of powdered tantalum occurred in the lungs of one healthy, anaesthetised dog after one inhalation via a tracheal cannula. Retention took place in the alveoli, and elimination of the dusts, which were deposited in the bronchia, occurred very rapidly within 25 hours. In the long term, the bronchial elimination from the alveolar deposition sites was evidently unimportant. The lymphogenic elimination was clearly more marked, though less than with comparable inert dusts (Wel73). By exposing (female) dogs via nose-only inhalation or intratracheal insufflation, for, usually, less than one hour, Bianco et al. also studied the lung clearance of tantalum aerosol dusts (mass mean aerodynamic diameter - MMAD: 4.0 μm; geometric standard deviation - GSD: 2.0 μm) using ^{182}Ta. All studies showed a rapid biphasic early tracheobronchial clearance phase and a later prolonged alveolar clearance phase with a mean biological half-life of greater than 2 years. The mucociliary transport was somewhat longer than that reported for other ‘insoluble’ dusts and, according to Bianco et al., it was apparently independent of the absolute amount of tantalum available (Bia74). Morrow et al. found pulmonary clearance of tantalum dusts following intratracheal insufflation into anaesthetised (female) dogs to be dependent on particle size: clearance half-lives were 2.1 years for particles with

MMADs of 3.6 μm (range: 1.5-4.9 μm; GSD: 1.9 μm) and 0.3 years for particles with MMADs of 6.8 (range: 5.0-8.0 μm; GSD: 2.2 μm) and 10 μm (range: 18-23 μm; GSD 2.6 μm). All particle sizes demonstrated rapid post-insufflation uptake by the pulmonary lymph nodes, followed either by retention or very slow clearance (Mor76).

Goering and Fowler (Goe91) reported that 'insoluble' $^{182}Ta_2O_5$ administered to rats by the oral route was poorly absorbed from the gastrointestinal tract with a total excretion in the faeces within 2 days. Oral administration of 'soluble' potassium tantalate in rats showed that ^{182}Ta was excreted rapidly and almost exclusively via the faeces; less than 2% of the dose was retained after 1 day. More than 96% of the administered dose was excreted after 3 days, less than 0.5% was recovered in the urine after 7 days, although more than 97% of the total dose had been excreted. Excretion of ^{182}Ta exhibited 3 phases: an early phase reflecting rapid excretion ($t_{1/2}$= 0.25 days) from the gastrointestinal tract of the unabsorbed compound, a second phase ($t_{1/2}$=2-5 days) which may reflect loss of ^{182}Ta that was loosely bound to tissues, and a third phase accounting for elimination of ^{182}Ta that had been absorbed and localised within tissues. This phase had a relative long biological half-life of 62 days in male and 119 days in female rats. After absorption, ^{182}Ta was primarily localised in bone compartment, which retained over 40% of the total body burden after 14 days. The highest concentrations of ^{182}Ta were found in the bone and kidney tissues.

Biological monitoring of workers occupationally exposed to hard metal dusts showed that tantalum concentrations in pubic hair or toenails might be useful as an indicator of exposure. By using neutron activation analysis, Sabbioni et al. found the following medians and ranges in 8 to 13 healthy workers: Ta in hair 94.5 ng/g (21.5-860 ng/g); Ta in toenails 235 ng/g (36-1590 ng/g); Ta in urine 1.1 μg/L (0.17-3.2 ng/L); and Ta in blood 0.9 μg/L (0.4-3 ng/L) (Sab94).

6 Effects and mechanism of action

Human data

There are a few case reports of dermatitis caused by contact to tantalum metal. Werman and Rietschel reported on a 39-year old woman with daily widespread urticarial lesions on the face, trunk, and extremities for 6 months. The personal history showed that due to recurrent deep vein phlebitis, femoral vein stripping had been performed. The earliest urticarial lesions had been found in and around the surgical scars. It was known, later, that the staples used in the surgery were composed entirely of tantalum. An intradermal test using tantalum solution

resulted in positive reactions (Wer81). Romaguera and Vilaplana reported on a 73-year-old man who had broken his left ankle and had consequently been fitted with a metal prosthesis consisting of Ti-Ta-Nb alloy. Two months later, exudative and extremely itchy, papular, erythematous, vesicular lesions appeared on the overlying skin. The lesions did not improve with treatment. A patch-test using 1% tantalum chloride gave a positive reaction (Rom95).

Animal data

The committee did not find data on the irritation and sensitisation properties of tantalum dusts on the respiratory tract and skin of experimental animals. Lauring and Wergeland reported that tantalum dusts with a diameter of less than 1.0 mm were well tolerated in the eyes of rabbits when placed into the mid-vitreous (Lau70). Limberger and Lenz also reported that tantalum is inert 12 weeks after being implanted in the subcutaneous tissue of the neck in rats (Lim91).

The oral LD_{50} in rats for tantalum oxide, tantalum chloride, and potassium tantalum fluoride were 8000, 1900, and 2500 mg/kg bw, respectively. The intraperitoneal LD_{50} of tantalum chloride and potassium tantalum fluoride in rats were 75 and 375 mg/kg bw, respectively. The intravenous LD_{50} of tantalum fluoride in mice was 110 mg/kg bw (Goe91).

Several experiments regarding the effects of tantalum dusts on the lungs are available. Morrow et al. exposed anaesthetised female dogs via intratracheal insufflation to radiolabelled tantalum dusts for usually less than one hour and examined them for up to 816 days post-exposure. Three different particle dimensions were studied: particles with MMADs of 3.6 µm (range: 1.5-4.9 µm; GSD: 1.9 µm), of 6.8 (range: 5.0-8.0 µm; GSD: 2.2 µm), and of 10 µm (range: 18-23 µm; GSD 2.6 µm). There was an initial rapid nodal uptake giving rise to a burden that either stayed relatively constant or slowly diminished. On histological examination of lung tissue, there was no evidence of pathological changes due to tantalum metal particles irrespective of the particle size, mass deposited, or the time of examination (Mor76). Weller and Kammler did not find cellular or fibrotic changes in the lungs and pulmonary lymph nodes of one male dog exposed to tantalum dust with a mean particle diameter of 5-10 µm (the concentration was not reported) once, at 18 months, the end of experiment (Wel73). A report of intratracheal instillation of tantalum oxide into 6 guinea pigs should be treated with caution. The author reported various effects on the lungs, but the technique of administration used in his experiment was very doubtful. Without using general anaesthesia, rupture of the lungs occurred in several cases (Del55). Scheepers used the same technique for instillation of a

10% suspension of 100 mg tantalum oxide dust in guinea pigs. He reported focal reactions. The aberrations found in the lungs comprised of acute and subacute bronchitis and bronchiolitis (Sch55). The committee concludes that the results of these intratracheal instillation experiments should be treated with caution since effects could be secondary.

Matthay et al. performed an *in vitro* experiment using rabbit alveolar macrophages. The effects of tantalum oxide were compared to silica and latex particles on the alveolar macrophages viability (evaluated by trypan blue exclusion test and release of cytoplasmic enzyme lactate dehydrogenase) and lysozome release over 30 hours. The results showed that all 3 sorts of particles were ingested by alveolar macrophages in culture, that tantalum oxide and silica were both toxic to alveolar macrophages *in vitro*, and that tantalum oxide exerted its toxic effects on alveolar macrophages less rapidly than did silica. From this experiment, Matthay et al. suggested that tantalum oxide might be toxic to alveolar macrophages *in vivo* (Mat78).

Heath et al. studied the carcinogenicity of various metals, including tantalum, in rats. Rats (n=10) were injected intramuscularly with 28 mg of powdered metallic tantalum. There was no obvious tissue reaction, and after 7 months, the rats were still alive and no tumours had appeared (Hea61).

Machlin et al. studied the reproduction toxicity of tantalum hydroxide by injecting doses of 1-80 mg into eggs containing 1- and 10-day chicken embryos. The results showed hypertrophy and degeneration of the kidneys of the embryos. According to Machlin et al., later work had shown that this was not a specific effect for the compound. In the dead embryos, haemorrhage of the developing vascular system was the most prominent (Mac52). The committee points out to the high doses used in this experiment; the LD_{50} in chicken eggs, as estimated by Machlin et al., was 44 mg for tantalum hydroxide.

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for tantalum in the Netherlands is 5 mg/m^3, 8-hour TWA.

Existing occupational exposure limits for tantalum in some European countries and in the USA are summarised in the annex.

8 Assessment of health hazard

Tantalum is an insoluble metal (dust) and very poorly absorbable by the lungs. Animal data have shown that the retention half-time in the lungs is more than a year. Long-term inhalation studies on experimental animals are not available and human data are limited to a few case-reports.

The committee considers the toxicological database on tantalum metal too poor to justify recommendation of a health-based occupational exposure limit.

The committee concludes that there is insufficient information to comment on the present MAC-value.

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Annex

Occupational exposure limits for tantalum in various countries.

country - organisation	occupational exposure limit		time-weighted average	type of exposure limit	note[a]	reference[b]
	ppm	mg/m^3				
the Netherlands						
- Ministry of Social Affairs and Employment	-	5	8 h	administrative		SZW04
Germany						
- AGS	-	6[c]	8 h			TRG03
	-	24[c]	15 min			
- DFG MAK-Kommission	-	4[c]	8 h			DFG03
	-	1,5[d]				
Great-Britain						
- HSE	-	5	8 h	OES		HSE02
		10	15 min			
Sweden	-	-				Swe00
Denmark	-	5	8 h	OEL		Arb02
USA						
- ACGIH	-	5	8 h	TLV		ACG04
- OSHA	-	5	8 h	PEL		ACG03
- NIOSH	-	5	10 h	REL		ACG03
		10	15 min			
European Union						
- SCOEL	-	-				EC04

[a] S = skin notation; which means that skin absorption may contribute considerably to body burden; sens = substance can cause sensitisation.

[b] Reference to the most recent official publication of occupational exposure limits.

[c] Measured as inhalable fraction.

[d] Measured as respirable fraction.