Magnesium carbonate

(CAS No: 546-93-0)

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 magnesium carbonate 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 MA Maclaine Pont, M.Sc. (Wageningen University and Research Centre, Wageningen, the Netherlands).

In May 2000, literature was searched in the databases Medline, Toxline, and Chemical Abstracts, starting from 1981, 1966, and 1937, and using the following key words: magnesium carbonate; magnesite; carbonic acid, compounds, magnesium salt (1:1); 546-93-0; or 13717-00-5. The final literature search was carried out in Toxline and Medline in January 2003.

In April 2003, the President of the Health Council released a draft of the document for public review. The committee received no comments.

2 Identity

name	:	magnesium carbonate
synonyms	:	magnesium (II) carbonate; carbonate magnesium; carbonic acid, magnesium salt (1:1); magnesite
molecular formula	:	$MgCO_3$
structural formula	:	-
CAS number	:	546-93-0

Data from ACG99, NLM02.

3 Physical and chemical properties

molecular weight	:	84.31
boiling point	:	900°C (liberating CO_2)
melting point	:	350°C (decomposes)
flash point	:	inflammable
vapour pressure	:	not available
solubility in water	:	insoluble (at 20°C: 0.01 g/100 mL)
log $P_{octanol/water}$	:	-2.12
conversion factors	:	not applicable

Data from ACG99, Lid 99, NLM02, http://esc.syrres.com.

Magnesium carbonate consists of odourless, white hexagonal crystals. It occurs naturally as the mineral magnesite, which is a white, yellowish, greyish-white, or brown crystalline solid, and as 3 hydrates: barringtonite ($MgCO_3.2H_2O$), landsfordite ($MgCO_3.5H_2O$), and nesquehonite ($MgCO_3.3H_2O$). In addition, there is a series of basic magnesium carbonates (Magnesia alba), having the general formula: $xMgCO_3.yMg(OH)_2.zH_2O$ (Bel94, Bud96, Cop81, Lid99).

4 Uses

Magnesite is used to make various grades of magnesium oxide, to produce carbon dioxide and refractories, as an additive to make free-running table salt, as a bulking compound in powder formulations, and as an antacid (ACG99). Magnesium carbonate is used as a filler for paper, in cosmetics and fire-resistant and insulating materials, and for clarifying drinking water. Magnesium carbonate boiled in water forms magnesia. Magnesia alba is used as an antacid and as a laxative (Bel94).

In 1985, the Food and Drug Administration of the USA affirmed in their final rule that certain magnesium salts, among which magnesium carbonate, are generally recognised as safe (GRAS) for use as direct human food ingredients (FDA85).

5 Biotransformation and kinetics

The committee did not find data on the toxicokinetics of magnesium carbonate.

6 Effects and mechanism of action

Human data

Magnesium is essential to both plants and animals. The body of an average adult contains about 25 g of magnesium. Magnesium is present in many foods, such as meats, cereals, vegetables, and milk. The average adult ingests about 300 mg of magnesium per day. Magnesium deficiency results in weakness, dizziness, and convulsions (Bel94). The daily requirement for adults is 2-3 mg (WHO81).

Magnesium is a normal constituent of human blood, being present at 1.6-2.2 meq/L. When serum magnesium reaches 3-4 meq/L, signs of central nervous sytem depression, loss of reflexes, muscular tone, and power, hypotension, and bradycardia may appear. Death in cardiac arrest and/or respiratory paralysis can occur when serum magnesium reaches 10-15 meq/L (ACG99).

Only a few epidemiological studies and findings of clinical investigations of magnesite-industry workers have been reported so far. The majority is written in Slovakian and published as proceedings of a conference. Reichrtová has summarised these data. A combined effect of $MgCO_3$ dust in mines and MgO dust in the environment has been described with respect to an increasing incidence of chronic bronchitis. A significant increase in the incidence of duodenal and gastric ulcers was found among magnesite-industry workers as a function of exposure duration. It is assumed that inhaled dust is partially ingested and thus finds its way to the digestive tract. Among workers involved in MgO production from magnesite, an approximately threefold increase was found in serum magnesium, incidence of pulmonary emphysema and chronic bronchitis, inflammation of nasal and ocular mucus, fatigue, and headache. In another study, impairment of upper airways and hearing was reported among magnesite-industry workers (Rei92). In other reports presented by ACGIH, cases of pneumoconiosis were document amongst others in a group of workers in a magnesite plant with 6 to 20 years of employment. Further, it was reported that complaints of coughing were rare among magnesite workers. The severity of the pneumoconiosis and complaints of coughing were found to be dependent on the crystalline silica content or asbestos content of the dust (ACG99).

Animal data

Magnesium carbonate was not irritating when tested in rabbits according to EC and French directives (Gau94). In evaluating alternative *in vitro* methods for screening eye irritancy, magnesium carbonate was concluded to be not to mildly irritating and not irritating in the bovine corneal opacity and permeability (BCOP) and hen's egg test-chorioallantoic membrane (HET-CAM) assay, respectively (Gau94, Gil96).

A single intratracheal instillation of 1 mL of a 7.5% suspension of magnesium carbonate (75 mg $MgCO_3$) in rats caused intense acute inflammatory reactions (no further data presented) (Hus52).

After a single intraperitoneal injection, magnesium carbonate did not induce adhesion of the abdominal wall in female Wistar rats at doses up to 100 mg. At doses up to 500 mg, there were no ascites or deposits of powder adherent to viscera. The authors concluded that magnesium carbonate is one of the least harmful powders out of 7 tested for use as dusting powder in condoms or surgical gloves (Kan92).

Carcinogenicity

Groups of male Fischer 344 rats were injected intrarenally with either vehicle (n=20), 2 doses of 5 mg of Ni_3S_2 (nickel subsulphide) (n=40), 2 doses of 6.2 mg of $4MgCO_3.Mg(OH)_2.nH_2O$ (magnesium basic carbonate, MgCarb) (n=20), or 2 doses of Ni_3S_2 plus MgCarb (n=20). After 109 weeks, no kidney tumours were found in the MgCarb group. Ni_3S_2 alone induced local renal tumours in 62.5% of the rats, with the first tumour appearing at week 30 after the injections. Ni_3S_2 carcinogenesis was strongly inhibited by MgCarb. The addition delayed the onset of renal tumours by 44 weeks and lowered the final yield of tumours to 20%. The authors did not have an explanation for the mode of action of magnesium (Kas94).

A similar experiment was performed by intramuscularly injecting male Fischer 344 rats with either 2.5 mg Ni_3S_2, or 6.1 mg MgCarb, or both doses combined, or with vehicle (in all cases: n=20). After 79 weeks, no sarcomas in the kidneys or metastases in lungs, kidneys, or other organs were found in the MgCarb group. In the Ni_3S_2 group, 100% of the animals had tumours, predominantly rhabdomyosarcomas. MgCarb inhibited the carcinogenicity of Ni_3S_2 in a dose-related manner. The final incidence of sarcomas decreased from 100% to 55%, and the appearance of first tumours was delayed from 25 to 39 weeks (Kas87).

Groups of 20 male F344 rats were given 5% L-ascorbic acid (AsA) (i.e., 2800 mg/kg/day*, or 3% $MgCO_3$ (i.e., 1500 mg/kg/day), or 5% AsA plus 3% $MgCO_3$ (i.e., 3200 and 1900 mg/kg/day, respectively), or none of these compounds via the diet for 32 weeks, following a 4-week pre-treatment with 0.05% of *N*-butyl-*N*-(4-hydroxybutyl)nitrosamine (BBN) via the drinking water. Groups of 5 male F344 rats received also AsA, $MgCO_3$, or AsA plus $MgCO_3$ via the food without pre-treatment with BBN (negative control groups). There was no increase in absolute urinary bladder weight or in the incidence of bladder papillary or nodular hyperplasia or papillomas or carcinomas (Fuk87).

Mutagenicity and genotoxicity

Magnesium carbonate was negative when tested - probably without metabolic activation - at only one concentration (50 mM) in a gene mutation assay using *S. typhimurium* strain TA102 (Cro96).

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* Calculated from an assumed mean body weight of 300 mg and data on average food intake presented in Fuk87.

Magnesium carbonate did not induce micronuclei in CHO cells or DNA-protein crosslinks in Balb/3T3 cells (concentration range: 0.6-2.4 µg/mL). Magnesium carbonate decreased the nickel-induced genotoxicity in CHO and Balb/3T3 cells (Hon97).

Reproduction toxicity

The committee did not find data on the potential reproduction toxicity of magnesium carbonate.

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for magnesium carbonate in the Netherlands is 10 mg/m^3, 8-hour TWA, as inhalable dust.

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

8 Assessment of health hazard

Magnesium is essential to both plants and animals, and recognised as safe for oral use as a direct human food ingredient, with a daily requirement for adults of 2-3 mg. Occupational inhalation exposure to unknown levels of, very probably, combined exposures of magnesium carbonate and magnesium oxide were reported to induce bronchitis, pulmonary emphysema, pneumoconiosis, nasal and ocular inflammation, fatigue, and headache in magnesite workers. In addition, co-exposure to crystalline silica and asbestos may have occurred as well, and in some studies, incidence and severity of the symptoms seemed to depend on the crystalline silica content or asbestos content of the dust. Therefore, the committee is of the opinion that the human data cannot be used for the assessment of the health effects of magnesium carbonate per se.

In long-term studies with rats, basic magnesium carbonate did not induce renal tumours or metastases in any organ; the compound inhibited the carcinogenic activity of nickel subsulphide (Ni_3S_2) in a dose-related manner (Kas87, Kas94). Magnesium carbonate did not affect the bladder of rats, after dosing via the food for 32 weeks, with an estimated intake of 1500 mg/kg bw/day (Fuk87).

The committee considers the lungs to be the target organ for toxicity.

Although the committee considers the toxicological database on magnesium carbonate too poor to justify recommendation of a health-based occupational exposure limit, the committee is of the opinion that the current occupational exposure limits of 5 and 10 mg/m^3 for respirable and inhalable dust, respectively, are acceptable for regulation of magnesium carbonate exposure.

In the presence of asbestos and crystalline silica, the legally binding MAC values of those substances have to be adhered to.

References

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EC03 European Commission: Directorate General of Employment and Social Affairs. Occupational exposure limits (OELs). http://europe.eu.int/comm/employment_social/h&s/areas/oels_en.htm.

FDA85 US Food and Drug Administration (FDA). GRAS status of magnesium carbonate, magnesium chloride, magnesium hydroxide, magnesium oxide, magnesium phosphate, magnesium stearate, and magnesium sulfate. Fed Reg 1985; 50: 13557-60.

Fuk87 Fukushima S, Shibata M, Shirai T, et al. Promotion by L-ascorbic acid of urinary bladder carcinogenesis in rats under conditions of increased urinary potassium ion concentration and pH. Cancer Res 1987; 47: 4821-4.

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NLM02 US National Library of Medicine (NLM), ed. Magnesium carbonate. In: Hazardous Substances Data Bank (HSDB) (last revision date magnesium carbonate file: May 13, 2002; last review date: September 29, 1994); http://toxnet.nlm.nih.gov.

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Swe00 Swedish National Board of Occupational Safety and Health. Occupational exposure limit values and measures against air contaminants. Solna, Sweden: National Board of Occupational Safety and Health, 2000; Ordinance AFS 2000:3.

SZW03 Ministerie van Sociale Zaken en Werkgelegenheid (SZW). Nationale MAC-lijst 2003. The Hague, the Netherlands: Sdu, Servicecentrum Uitgevers, 2003: 33.

TRG00 TRGS 900. Grenzwerte in der Luft am Arbeitsplatz; Technische Regeln für Gefahrstoffe. BArbBl 2000; 2.

WHO81 World Health Organization: International Programme on Chemical Safety (WHO/IPCS). Manganese. Geneva, Switzerland: WHO, 1981; Environmental Health Criteria 17.

Annex

Occupational exposure limits for magnesium carbonate 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	-	10[c]	8 h	administrative		SZW03
Germany						
- AGS	-	-				TRG00
- DFG MAK-Kommission	-	-				DFG02
Great Britain						
- HSE	-	10[c]; 4[d]	8 h	OES		HSE02
Sweden	-	-				Swe00
Denmark	-	-				Arb02
USA						
- ACGIH	-	10[e]	8 h	TLV		ACG03b
- OSHA	-	15[c]; 5[d]	15 min	PEL		ACG03a
- NIOSH	-	10[c]; 5[d]	8 h	REL		ACG03a
European Union						
- SCOEL	-	-				EC03

[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] As (total) inhalable dust.
[d] As respirable dust.
[e] The value is for particulate matter containing no asbestos and <1% crystalline silica.