Calcium hydroxide

(CAS No: 1305-62-0)

Health-based Reassessment of Administrative Occupational Exposure Limits

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

No. 2000/15OSH/096 The Hague, March 30, 2004

Preferred citation:
Health Council of the Netherlands: Committee on Updating of Occupational Exposure Limits. Calcium hydroxide; Health-based Reassessment of Administrative Occupational Exposure Limits. The Hague: Health Council of the Netherlands, 2004; 2000/15OSH/096.

1 Introduction

The present document contains the assessment of the health hazard of calcium hydroxide 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 C de Heer, Ph.D. and H Stouten, M.Sc. (TNO Nutrition and Food Research, Zeist, the Netherlands).

The evaluation of the toxicity of calcium hydroxide has been based on the review by the American Conference of Governmental Industrial Hygienists (ACGIH) (ACG91). Where relevant, the original publications were reviewed and evaluated as will be indicated in the text. In addition, in May 1998, literature was searched in the on-line databases Medline, Toxline, and Chemical Abstracts starting from 1966, 1965, and 1967, respectively, and using the following key words: calcium hydroxide, calcinosis, and 1305-62-2.

In March 2000, the President of the Health Council released a draft of the document for public review. The committee received comments by the following individuals and organisations: A Aalto (Ministry of Social Affairs and Health, Tampere, Finland) and P Wardenbach, Ph.D. (Bundesanstalt für Arbeitsschutz and Arbeitsmedizin, Dortmund, FRG). These comments were taken into account when deciding on the final version of the document.

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

2 Identity

name	:	calcium hydroxide
synonyms		calcium dihydroxide; calcium hydrate; carboxide; hydrated lime; slaked lime; caustic lime; lime milk; lime water
molecular formula	:	CaH_2O_2
structural formula		$Ca(OH)_2$
CAS number	:	1305-62-0

3 Physical and chemical properties

molecular weight	:	74.09
boiling point	:	-
melting point	:	decomposes at 580ºC (dehydrates to form CaO)
flash point	:	not flammable
vapour pressure	:	-
solubility in water	:	slightly soluble (at 20ºC: 1.7 g/100 mL)
log $P_{octanol/water}$	:	-0.87 (estimated)
conversion factors	:	not applicable

Data from ACG91, EC03a*, NLM03, http://esc.syrres.com.

Calcium hydroxide is a soft, white, odourless, crystalline powder with an alkaline bitter taste.

4 Uses

Calcium hydroxide has many industrial applications. Its major uses are in mortar, plaster, cement, and other building and paving materials. It is also used in lubricants, drilling fluids, fireproofing coatings, and pesticides, in the manufacture of paper pulp, in dehairing animal hides, in water and sewage treatment, in flue gas purification, and, in the chemical industry, as a scrubbing and neutralising agent (ACG91, EC03a).
In routine dental practice, calcium hydroxide is used as a constituent of root canal sealers (Eco95).

5 Biotransformation and kinetics

The committee did not find data on the kinetics of calcium hydroxide.

6 Effects and mechanism of action

Human data

Acute exposures to calcium hydroxide may cause irritation, along with coughing, pain, and possibly burns of the mucous membranes with, in severe acute

* See remark in ‘References’.

exposures, pulmonary oedema and hypotension with weak and rapid pulse (Pie93, Ric93). There are numerous case reports on accidental exposures to calcium hydroxide resulting in corneal and skin alkali burns and caustic ulcers (e.g., Ear85, Fis85, Gel92, Koo92, Kuc93, Luo95, OGr89). Generally, these effects are caused by the solid material and less commonly or rarely by solutions (see EC03a).

Ingestion of alkali is reported to be followed by severe pain, vomiting (containing blood and desquamated mucosal lining), diarrhoea, and collapse. If death does not occur within the first 24 hours, the patient may improve in 2-4 days (EC03a, NLM03).

According to (not documented) statements in ACG91 and EC03a, 'epidemiological syndromes' related to lime exposure during production and application are not known, and workers in lime factories exposed to lime for up to 40 years have not experienced adverse effects.

In an explorative epidemiological study, mortality was studied by multiple testing in 607 male cement workers employed in 1939 in England and Wales. Person-years at risk were calculated from 1948-1981. Expected numbers of deaths for the causes of death analysed were calculated on the basis of the corresponding male mortality rates for England and Wales. The standardised mortality ratio (SMR) for stomach cancer was significantly raised in the overall cohort (SMR 175, based on 22 deaths), was significantly increased under control of social class, and was associated with an index of cement plant dust exposure (McD84). However, no information was available on latency and tenure, and a surrogate measure of cement plant dust exposure was employed (job held in 1939) which is not an accurate surrogate measure of cumulative or average respirable dust exposure.

In another study, the mortality from stomach cancer of United States cement plant and quarry workers was addressed. A cohort of 5292 men who had been employed for at least 5 years in a non-asbestos cement plant between 1950 and 1960 was traced to 1 January 1980. The mortality experience was evaluated for 4231 white men for whom complete work histories and demographic information were available. The expected number of deaths was computed using age-year specific death rates from the United States white male population. Deaths from stomach cancer were significantly increased during 1965-1969, but not over the entire follow-up period (1950-1980) (SMR 135, based on 27 deaths). Additionally, stomach cancer mortality was not significantly associated with tenure under separate control for age at follow-up, latency, nativity, or year of birth (Ama86). Amandus concluded that there is no association between exposure to cement-plant dust and death from stomach cancer possibly because

of the low statistical power. Therefore, a conclusion awaits a study with a sufficient number of cases with information on gastric-cancer risk factors.

Based on the available data, McDowell concluded that epidemiological evidence is insufficient to reach any definite conclusions on the association between cement-dust exposure and stomach cancer (McD86).

Chronic oral exposures may cause inflammatory and ulcerative changes in the mouth and gastrointestinal problems (Pie93).

Betel-quid chewing is a popular habit in Southeast Asian countries held responsible for the very high incidence of oral cancers in these areas (Jen94, Kiy92, Tho92). Although the composition of betel quid varies in different geographic locations, it generally consists of betel nut (*Areca catechu*), *Piper betle* leaf, and slaked lime (calcium hydroxide) with or without tobacco. Aqueous extracts of such lime (50-800 μg/mL) increased proliferation of oral mucosal fibroblasts *in vitro* by 20-40% (Jen94), but did not induce cytotoxicity (up to concentrations of 800 μg/mL) or DNA strand breaks (at concentrations up to 3 mg/mL). The site of oral squamous cell tumours in betel-quid chewers corresponded strongly ($p<0.0001$) with the predominant site of contact with slaked lime (Jen94). Therefore, reactive oxygen species from betel-quid ingredients together with sustained lime-induced cell proliferation was suggested as a possible mechanism underlying the induction of these tumours (Jen94, Kiy92, Tho92). However, the relevance of these epidemiological observations for the evaluation of calcium hydroxide carcinogenicity is questionable because in addition to calcium hydroxide, lime also consists of secret seasoning additives (Jen94).

Animal data

Calcium hydroxide was reported not to be irritating in rabbits when tested according to OECD guideline 404 (acute dermal irritation/corrosion), but no reference to a particular study was made (EC03a). It was stated not to be sensitising (no reference given) (EC03a). When placed as a dry powder (10-100 mg) on the cornea of rabbits (Draize test), calcium hydroxide was corrosive (Gri80). Rabbits exposed for 1 minute to a paste of calcium hydroxide in the eyes followed by cleaning and rinsing with a physiological salt solution displayed a gradual decrease in mucopolysaccharides of the cornea, reaching a maximum at 24 hours, which did not return to normal levels within 3 months (Pie93).

The oral LD_{50} values in rats and mice were 7340 and 7300 mg/kg bw, respectively (NIO03, Smy69).

The long-term exposure (70-98 weeks, 3-5 times/week) of the cheek pouch to several ingredients of betel quid was studied in Syrian hamsters. It was shown that repeated applications of calcium hydroxide (50 mg, alone or in combination with other ingredients) severely injured the hamster cheek pouch. Three of the inflammatory and hyperplastic lesions that developed in the pouches of 26 calcium hydroxide-treated hamsters progressed to epithelial atypia (Dun66).

In male rats, subchronic exposure to calcium hydroxide in drinking water (50 and 350 mg/l)* for 3 months resulted in restlessness, aggression, reduced food intake, and body weight loss. In addition, decreased counts for erythrocytes and phagocytes, and decreased haemoglobin were noted. At sacrifice, gross necropsy showed inflammation of the small intestine and dystrophic changes in the stomach, kidneys, and liver (Pie93, EC03a).

The committee did not find data from genotoxicity, mutagenicity, reproduction and developmental toxicity studies.

7 Existing guidelines

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

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

8 Assessment of health hazard

Solid calcium hydroxide is corrosive to the eyes and may cause severe injury to the skin. Aqueous solutions are (far) less irritating. There are no adequate human data from which inhalation exposure concentration-effect relationships can be derived. Two epidemiological studies that addressed the association between cement-dust exposure and stomach cancer were considered insufficient to reach any conclusions on the association between cement dust exposure and stomach cancer (McD84, McD86). However, no adverse effects have been experienced by long-term exposed workers.

Oral LD_{50} values of approximately 7300 mg/kg bw were reported for rats and mice. No adequate repeated-dose toxicity (including carcinogenicity and reproduction toxicity) or genotoxicity/mutagenicity studies were available.

* Equivalent to 5 and 35 mg/kg bw/day, assuming a daily water consumption of 25 mL and a body weight of 250 g.

Because of the likely occurrence of local effects, repeated inhalation studies would be the preferred type of study.

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

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

References

ACG91 American Conference of Governmental Industrial Hygienists (ACGIH). Calcium hydroxide. In: Documentation of the threshold limit values and biological exposure indices. 6th ed. Cincinnati OH, USA; ACGIH®, Inc, 1991: 199.

ACG03a American Conference of Governmental Industrial Hygienists (ACGIH). Guide to occupational exposure values - 2003. Cincinnati OH, USA: ACGIH®, Inc, 2003: 21.

ACG03b American Conference of Governmental Industrial Hygienists (ACGIH). 2003 TLVs® and BEIs® based on the documentation of the Threshold Limit Values for chemical substances and physical agents & Biological Exposure Indices. Cincinnati OH, USA: ACGIH®, Inc, 2003: 19.

Ama86 Amandus HE. Mortality from stomach cancer in United States cement plant and quarry workers, 1950-80. Br J Ind Med 1986; 43: 526-8.

Arb02 Arbejdstilsynet. Grænseværdier for stoffer og materialer. Copenhagen, Denmark: Arbejdstilsynet, 2002: 19 (At-vejledning C.1.0).

DFG03 Deutsche Forschungsgemeinschaft (DFG): Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area. List of MAK and BAT values 2003. Maximum concentrations and Biological Tolerance Values at the workplace Weinheim, FRG: Wiley-VCH Verlag GmbH & Co. KGaA, 2003; rep no 39.

Dun66 Dunham LJ, Muir CS, Hamner JE III. Epithelial atypia in hamster cheek pouches treated repeatedly with calcium hydroxide. Br J Cancer 1966; 20: 588-93.

Ear85 Early SH, Simpson RL. Caustic burns from contact with wet cement. JAMA 1985; 254: 528-9.

EC03a European Commission (EC): European Chemicals Bureau (ECB). IUCLID Dataset - calcium hydroxide. In: Public data on high volume chemicals IUCLID CD-ROM. Year 2000 ed. Ispra, Italy: European Commission, Joint Research Centre, Institute for Health and Consumer Protection, European Chemicals Bureau, 2000*.

* This dossier is a compilation based on data reported by the European Chemicals Industry following 'Council Regulation (EEC) No 793/93 on the Evaluation and Control of the Risks of Existing substances' to allow a risk assessment by member states of the EC. However, the data in the dossier have not undergone any evaluation by any EC member state yet.

EC03b 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.

Eco95 Economides N, Kotsaki-Kovatsi VP, Poulopoulos A, et al. Experimental study of the biocompatibility of four root canal sealers and their influence on the zinc and calcium content of several tissues. J Endod 1995; 21: 122-7.

Fis86 Fischer G, Commens C. Cement burns: rare or rarely reported? Australas J Dermatol 1986; 27: 8-10.

Gel92 Gelmetti C, Cecca E. Caustic ulcers caused by calcium hydroxide in 2 adolescent football players. Contact Dermatitis 1992; 27: 265-6.

Gri80 Griffith JF, Nixon GA, Bruce RD, et al. Dose-response studies with chemical irritants in the albino rabbit eye as a basis for selecting optimum testing conditions for predicting hazard to the human eye. Toxicol Appl Pharmacol 1980; 55: 501-13.

HSE02 Health and Safety Executive (HSE). EH40/2002. Occupational Exposure Limits 2002. Sudbury (Suffolk), UK: HSE Books, 2002: 14.

Jen94 Jeng JH, Kuo ML, Hahn LJ, et al. Genotoxic and non-genotoxic effects of betel quid ingredients on oral mucosal fibroblasts in vitro. J Dent Res 1994; 73: 1043-9.

Kiy92 Kiyingi KS. Slaked lime and betel nut cancer in Papua New Guinea. (Letter). Lancet 1992; 340: 1357-8.

Koo92 Koo CC, Morgan BDG, Parkhouse N. Cement water - the hidden hazard. Burns 1992; 18: 513-4.

Kuc93 Kuckelkorn R, Makropoulos W, Kottek A, et al. Retrospektive Betrachtung von schweren Alkaliverätzungen der Augen. Klin Mbl Augenheilk 1993; 203: 397-402.

Luo95 Luong KVQ, Nguyen LTH. Cement burn. J Fam Pract 1995; 41: 601-2.

McD84 McDowall ME. A mortality study of cement workers. Br J Ind Med 1984; 41: 179-82.

McD86 McDowall M. Cement workers and cancer: epidemiology at work? Br J Ind Med 1986; 43: 505-6.

NIO03 US National Institute for Occupational Safety and Health (NIOSH), ed. Calcium hydroxide. In: Registry of Toxic Effects of Chemical Substances (RTECS) (last update calcium hydroxide file: October 2002); http://www.cdc.gov/niosh.

NLM03 US National Library of Medicine (NLM), ed. Calcium hydroxide. In: Hazardous Substances Data Bank (HSDB) (last revision data calcium hydroxide file: March 2003; last review date: September 1994); http://toxnet.nlm.nih.gov.

OGr89 O'Grady TC. Mass eye casualties at sea. Mil Med 1989; 154: 596-8.

Pie93 Pierce JO. Alkaline materials. In: Clayton GD, Clayton FE, eds. Toxicology. 4th ed. New York: John Wiley & Sons, 1993: 762-4. (Patty's industrial hygiene and toxicology; Vol II, Pt A).

Ric93 Richardson ML, Gangolli S, eds. C31 Calcium hydroxide. In: The dictionary of substances and their effects. Cambridge, UK: Royal Society of Chemistry, 1993: 53-4 (Vol 2).

Smy69 Smyth HF Jr, Carpenter CP, Weil CS, et al. Range-finding toxicity data: list VII. Am Ind Hyg Assoc J 1969; 30: 470-6.

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: 20.

Tho92 Thomas SJ, MacLennan R. Slaked lime and betel nut cancer in Papua New Guinea. Lancet 1992; 340: 577-8.

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

Annex

Occupational exposure limits for calcium hydroxide 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	-	5	8 h	administrative		SZW03
Employment	-	-				
Germany						
- AGS	-	5[c]	8 h			TRG00
- DFG MAK-Kommission	-	-				DFG03
Great-Britain						
- HSE	-	5	8 h	OES		HSE03
Sweden	-	-				Swe00
Denmark	-	5	8 h			Arb02
USA						
- ACGIH	-	5	8 h	TLV		ACG03b
- OSHA	-	5[d]	8 h	PEL		ACG03a
	-	15[e]	8h			
- NIOSH	-	5	10 h	REL		ACG03a
European Union						
- SCOEL	-	5		ILV[f]		EC03b

[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] Inhalable dust.
[d] Respirable fraction.
[e] Total dust.
[f] Listed among compounds for which OELs are already included in Commission Directives.