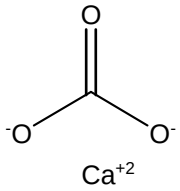
CALCIUM CARBONATE

SYNONYMS

Aeromatt
Calcene
Calofil
Calopake
Chalk
Durcal
Eskalon
Hakuenka
Neolite
Omya
Snowcal
Socal
Sturcal
Vicron
Whitton

CHEMICAL STRUCTURE



CHEMICAL FORMULA

$CaCO_3$

IDENTIFIER DETAILS

CAS Number	:	471-34-1
CoE Number	:	-
FEMA	:	-
EINECS Number	:	207-439-9
E Number	:	E170

CLP CLASSIFICATION

Ingredient CLP Classification: No

Endpoint	Classification	Category
Acute Oral Toxicity	-	-
Acute Dermal Toxicity	-	-
Acute Inhalation Toxicity	-	-
Skin Corrosive/irritant	-	-
Eye Damage/Irritation	-	-
Respiratory Sensitisation	-	-
Skin Sensitisation	-	-
Mutagenicity/Genotoxicity	-	-
Carcinogenicity	-	-
Reproductive Toxicity	-	-
Specific Target Organ Toxicity	-	-
Aspiration Toxicity	-	-

REACH Statement

This ingredient has been registered under REACH. Under REACH, registrants have an obligation to provide information on substances they manufacture or import. This information includes data on hazardous properties (covering various toxicological endpoints), guidance on safe use and classification and labelling. The European Chemicals Agency (ECHA) makes this information publicly available on its website: http://echa.europa.eu/.

SPECIFICATIONS

Melting Point: 825 °C

Boiling point: Decomposes upon further heating

PURPOSE

Tobacco paper filler; potential colouring agent

STATUS IN FOOD AND DRUG LAWS

CoE limits:

Beverages (mg/kg)	Food (mg/kg)	Exceptions (mg/kg)

Acceptable Daily Intake:

ADI (mg/kg)	ADI Set by	Date Set	Comments
NOT LIMITED	JECFA	1967	

FDA Status:[CFR21]

Section Number	Comments
184.1190*	GRAS

HUMAN EXPOSURE

Natural Occurrence: Calcium carbonate is an odourless, tasteless powder or crystal that occurs widely in nature [HSDB, 1999].

Reported Uses: The main use of calcium carbonate is in the construction industry, either as a building material in its own right (e.g. marble), limestone aggregate for road building, an ingredient of cement or as the starting material for the preparation of builder's lime by burning in a kiln.

Calcium carbonate is widely used as an extender in paints, in particular matt emulsion paint where typically 30% by weight of the paint is either chalk or marble.

Calcium carbonate is also widely used as a filler in plastics. Some typical examples include around 15 to 20% loading of chalk in uPVC drain pipe, 5 to 15% loading of stearate coated chalk or marble in uPVC window profile. Fine ground calcium carbonate is an essential ingredient in the microporous film used in babies' nappies and some building films as the pores are nucleated around the calcium carbonate particles during the manufacture of the film by biaxial stretching.

Calcium carbonate is also used in a wide range of trade and DIY adhesives, sealants and decorating fillers. Ceramic tile adhesives typically contain 70 to 80% limestone. Decorating crack fillers contain similar levels of marble or dolomite.

Calcium carbonate is widely used medicinally as an inexpensive calcium supplement, antacid, and/or phosphate binder. It is also used in the pharmaceutical industry as a base material for tablets of other pharmaceuticals.

As a food additive, it is used in some soy milk products as a source of dietary calcium

Sources other than foods: Calcium carbonate is reportedly used therapeutically as a phosphate buffer in haemodialysis patients, as a calcium supplement, as an antacid, and as an anti-diarrhoeal agent [HSDB, 1999].

TOXICITY DATA

In Vivo Toxicity Status

Species	Test Type	Route	Reported Dosage
Rat	LD_{50}	Oral	6450mg/kg [HSDB, 1999]

Rat	Irritation (moderate)	Dermal	500mg/24 hours
Rabbit	Irritation (severe)	Ocular	750ug/kg/24 hours
			[NISC 2003]

Calcium is an essential mineral, with an average 70 kg human containing 1 kg calcium. Calcium may affect bone formation/resorption, protein absorption and mineral absorption. It is reported that any specific [unspecified] adverse toxicological outcome concerning calcium carbonate is in fact associated with the Ca^{2+} ion. If injected subcutaneously or intramuscularly (dose levels unspecified in humans) it acts as an irritant. If injected intravenously it causes slowing of the heart rate, extrasystole, and ventricular fibrillation. If taken orally (amounts not specified in humans) it leads to gastric irritation by disturbing osmotic processes. It has been associated with the lowering of blood cholesterol levels and it has been postulated that it may have a protective effect against colon cancer [Gosselin *et al.,* 1984].

Limited animal data concerning calcium toxicity has been reported in both rats and dogs. Administration of excess calcium can lead to a reduced filtration rate, enlarged kidneys and kidney calcification [Report by the Expert Group on Vitamins and Minerals, 2003].

Carcinogenicity and Mutagenicity

An animal model of gastric resection was used to investigate the effects of calcium carbonate on spontaneous development of gastric adenocarcinoma. The carcinogenic potential of calcium carbonate supplements in food was investigated in Wistar rats (92 rats with gastric resections to induce spontaneous gastric cancer and 60 control rats) over a period of 10 months. Tumours developed in 3 out of 18 (17 %) of resected rats given 5 % w/v (i.e. 7 times normal amount in diet) sodium chloride (NaCl), 11 out of 18 (61 %) of the resected rats exposed to 2.2 % w/v (2.2% Ca^{2+} i.e. 2 times normal amount in diet and 3.3 % CO_3^{2-}) calcium carbonate ($CaCO_3$), but no tumours developed in the unresected rats. Differentiation between the carcinogenic potential of calcium or the carbonate was also investigated. Out of 26 resected rats exposed to dicalcium phosphate dehydrate ($CaHPO_4$) (2.2 % Ca^{2+} w/v), only 1 (4 %) rat developed tumours, whereas 13 out of 24 (54 %) rats developed tumours when fed a diet supplemented with sodium hydrogen carbonate ($NaHCO_3$) (3.3 % CO_3^{2-}). It was concluded that carbonate maybe significant in the induction of gastric carcinoma in the rat (Ehrnström *et al*., 2006).

Reproductive and Developmental Toxicity

One study looked at excess dietary Ca^{2+} supplementation in rats at 0.5 (control), 0.75, 1.0 or 1.25% to see if it had any affect on foetal development. Under the conditions of the study (modified AIN-76A diet supplemented with calcium) it had no maternal toxic effects, and was neither foetotoxic nor teratogenic at concentrations of up to 1.25% calcium carbonate in the diet. [Shackelford *et al.,* 1993].

A study that examined the effects of feeding pregnant mice with 8.2% calcium as both the carbonate and lactate (approximating to 12,200 mg/kg/day), compared to the controls that received 1.2% calcium (approximating to 1800 mg/kg/day) lead to significantly reduced foetal weights, retarded skeletal and dental calcification. There was reported to be no gross foetal abnormalities [Report by the Expert Group on Vitamins and Minerals, 2003].

Another study reported that rats maintained on a high calcium diet (estimated to be 12,200 mg/kg/day) throughout pregnancy and lactation of pups, the pups were born slightly hypocalcaemia. It had no maternal toxic effects, and was neither foetotoxic nor teratogenic. Pups were reported to have reduced growth rates and focal alopecia. On returning the pups to a normal diet, all the findings were found to be reversible [Report by the Expert Group on Vitamins and Minerals, 2003].

Inhalation Toxicity

The addition of calcium carbonate at 9000 ppm to reference cigarettes, used in a 90 day-sub-chronic inhalation exposure in rats, led to a series of pathological changes to smoke exposure that were indistinguishable from those changes caused by the control cigarettes. This indicated that addition of calcium carbonate to a reference cigarette had no discernable effect upon the type or severity of the treatment related pathological changes associated with tobacco smoke exposure [Baker *et al.,* 2004]

Other relevant studies

The calcium intake for healthy bone formation and skeletal growth increases between the years of 1-18. The reference nutrition intake (RNI) for children aged 1-3, 4-6, 7-10 and 11-18 are 350, 450, 550, 800 (females) and 1000 mg/day (males) respectively. The recommended level for adults is 700 mg/day, which represents the rates of calcium loss and retention per day [Report by the Expert Group on Vitamins and Minerals 2003].

In some but not all studies, calcium supplementation (1250-2000 mg/day) has been reported to reduce colic and rectal cell proliferation in those humans at an increased risk from developing colon cancer. It has also been suggested by epidemiological studies that dietary calcium may improve hypertension in non pregnant women. There has also been studies to indicate that increased calcium intake is associated with decreased blood pressure in children [Report by the Expert Group on Vitamins and Minerals, 2003].

Calcium fulfils an important physiological role in the bodies of mammals being an important cofactor for many enzyme systems, and is an important component of the blood clotting system. Calcium deficiency is associated with symptoms manifested in the bones and teeth, resulting in poor quality bone and teeth with stunted and/or malformed bone growth. However, excessive calcium intake (serum concentrations above 10.5 mg/dl) may lead to hypocalcaemia. This is characterised by progressive lethargy, leading to

confusion and ultimately coma (serum concentrations above 14 mg/dl). Hypercalcaemia is reported to occur more frequently with excessive ingestion of both calcium and an alkali, such as antacids, milk (which contains vitamin D that improves the absorption of calcium) or calcium supplements. The condition is commonly known as milk alkali syndrome (MAS) . [Report by the Expert Group on Vitamins and Minerals, 2003].

A slight to moderate metabolic alkalosis occurs during treatment [human] with calcium carbonate, but is slow to develop. When hypercalcaermia is evident, calcinosis/nephrocalcinosis can occur infrequently. However, normal individuals can ingest up to 20 g/day without developing hypercalcaemia [HSDB, 1999]. The clinical signs of MAS are hypercalcaemia, renal insufficiency and alkalosis. Acute and intermediate MAS the symptoms are reported to be reversible, however, chronic MAS is associated with only partial or non reversible renal insufficiency and metastatic calcification (deposition of calcium in soft tissues) [Report by the Expert Group on Vitamins and Minerals, 2003].

It has been reported that in numerous human clinical trials, calcium carbonate supplements (250-2000 mg/day), were given to patients with a history of adenomatous colonic polyps, for periods from 4 weeks up to 4 years of duration. There were few side effects reported as this was not the aim of the clinical trials in question. It has been reported that in those studies where dosages were high enough for clinical signs, these were described to be a low incidence of gastrointestinal effects including severe abdominal pain and/or diarrhoea [Report by the Expert Group on Vitamins and Minerals, 2003].

The risk of coronary and cerebrovascular events was evaluated in a randomised trial of 36,282 post-menopausal women aged 50 to 79 years of age given 500 mg calcium carbonate with vitamin D 200 IU, or a placebo, twice daily. After 7 years, myocardial infarction or coronary heart disease was confirmed for 499 women given the calcium carbonate/vitamin D supplements and 475 women given the placebo. Stroke was confirmed in 362 women given supplements and 377 given the placebo. It was concluded that supplementation of the diet with calcium carbonate/vitamin D does not have appear to have an impact upon coronary or cerebrovascular risk in generally healthy menopausal women (Hsia *et al*., 2007).

Behavioural Data

No data identified

***In Vitro* Toxicity Status**

Carcinogenicity and Mutagenicity

Fujita *et al*., (1987) carried out an Ames assay using *Salmonella typhimurium* strains TA97 and TA102 with and without S9 metabolic activation. All results were negative [Fujita *et al*., 1987].

Baker *et al.,* [2004]; examined the effects of the addition of 482 tobacco ingredients upon the biological activity and chemistry of mainstream smoke. The ingredients, essentially different groups of flavourings and casings, were added in different combinations to reference cigarettes. The addition of calcium carbonate at 9000 ppm was determined to not affect the mutagenicity of the total particulate matter (TPM) of the smoke in either the Ames, *in vitro* micronucleus assay or the neutral red assay when compared with that of the control cigarettes [Baker *et al.,* 2004].

Additional information concerning the *in vitro* mutagenicity of this material may be found in "An Interim report on data originating from Imperial Tobacco Limited's Genotoxicity testing programme September 2003" or "An updated report on data originating from Imperial Tobacco Limited's external Genotoxicity testing programme – Round 2 August 2007".

REFERENCES

Baker RR, *et al.,* (2004) An overview of the effects of tobacco ingredients on smoke chemistry and toxicity. *Food Chem Toxicol*. **42** Suppl: S53-83.

Ehrnstrom RA, Veress B, Arvidsson S, Sternby NH, Andersson T, Lindstrom CG (2006).Dietary supplementation of carbonate promotes spontaneous tumorigenesis in a rat gastric stump model. *Scand J Gastroenterol*. 41(1):12-20.

Fujita *et al*., (1987). Mutagenicity test of food additives with *Salmonella typhimurium* TA97 and TA102. [Japanese] *Kenkyu Nenpo – Tokyo-Toritsu Eisei Kenkyusho*, **38**, 423 – 430.

Gosselin *et al.*, (1984). Clinical toxicology of commercial products. 5th Edition. Ed. T. M. Tracy. Williams & Wilkins, Baltimore.

Hazardous Substances Databank [HSDB] (1999)– Calcium carbonate: via TOXNET, US National Library of Medicine.

Hsia J, Heiss G, Ren H, Allison M, Dolan NC, Greenland P, Heckbert SR, Johnson KC, Manson JE, Sidney S, Trevisan M. (2007) Calcium/vitamin D supplementation and cardiovascular events. *Circulation*. **115**(7):846-54.

Report by the Expert Group on Vitamins and Minerals (2003) Safe upper levels for vitamins and minerals http://www.foodstandards.gov.uk/multimedia/pdfs/vitmin2003.pdf

Shackelford *et al.,* (1993). Foetal development in rats fed AIN-76A diets supplemented with excess calcium. *Fd. Cosmet. Toxicol.*, **31**, 953.