### Calcium Glycerophosphate

Calcii glycerophosphas; Calcio, glicerofosfato de; Calcium Glycerinophosphate; Calcium, glycérophosphate de; Calcium Glycerylphosphate; Glycerofosforečnan vápenatý; Kalcio glicerofosfatas; Kalcium-glicerofoszfát; Kalciumglycerofosfat; Kalsiumglyserofos-

 $C_3H_7CaO_6P(+xH_2O) = 210.1$  (anhydrous). CAS — 27214-00-2 (anhydrous calcium glycerophos-CĂS' phate). - A I 2AA08.

ATC Vet - QA I 2AA08.

Pharmacopoeias. In Eur. (see p.vii), US., and Viet.

Ph. Eur. 6.2 (Calcium Glycerophosphate). A mixture in variable proportions of calcium (RS)-2,3-dihydroxypropyl phosphate and calcium 2-hydroxy-1-(hydroxymethyl)ethyl phosphate, which may be hydrated. It contains not less than 18.6% and not more than 19.4% of calcium, calculated with reference to the dried substance. A white or almost white, hygroscopic powder. Sparingly soluble in water: practically insoluble in alcohol. It loses not more than 12% of its weight on drying.

USP 31 (Calcium Glycerophosphate). A mixture, in variable proportions, of calcium (RS)-2,3-dihydroxypropyl phosphate and calcium 2-hydroxy-1-(hydroxymethyl)ethyl phosphate, which may be hydrated. It contains not less than 18.6% and not more than 19.4% of calcium, calculated with reference to the dried substance. Store at a temperature between 20° and 25°, excursions permitted between 15° and 30°.

**Equivalence.** Each g of calcium glycerophosphate (anhydrous) represents about 4.8 mmol of calcium. Calcium glycerophosphate (anhydrous) 5.24 g is equivalent to about 1 g of calcium.

## Calcium Hydrogen Phosphate

Calcii et Hydrogenii Phosphas; Calcii hydrogenophosphas; Calcio, hidrogenofosfato de; Calcium, hydrogénophosphate de; Calcium Hydrophosphoricum; Calcium Monohydrogen Phosphate; Dicalcium Orthophosphate; Dicalcium Phosphate; E341; Hydrogenfosforečnan vápenatý; Kalcio-vandenilio fosfatas; Kalcium-hidrogén-foszfát; Kalciumvätefosfat; Kalsiumvetyfosfaatti; Wapna wodorofosforan. Calcium hydrogen orthophosphate.

CaHPO $_4$  = 136.1 (anhydrous); 172.1 (dihydrate). CAS — 7757-93-9 (anhydrous calcium hydrogen phosphate); 7789-77-7 (calcium hydrogen phosphate dihy-

**Pharmacopoeias.** In Chin., Eur. (see p.vii), Int., Jpn, and US, which includes monographs for the anhydrous substance and the dihydrate form.

Ph. Eur. 6.2 (Calcium Hydrogen Phosphate, Anhydrous; Calcii Hydrogenophosphas Anhydricus). A white or almost white, crystalline powder, or colourless crystals. Practically insoluble in water and in alcohol; dissolves in dilute hydrochloric acid and in dilute nitric acid

Ph. Eur. 6.2 (Calcium Hydrogen Phosphate Dihydrate; Calcii Hydrogenophosphas Dihydricus; Calcium Hydrogen Phosphate BP 2008). A white or almost white, crystalline powder. Practically insoluble in cold water and in alcohol; dissolves in dilute hydrochloric acid and in dilute nitric acid.

The BP 2008 gives Dibasic Calcium Phosphate as an approved

**USP 31** (Anhydrous Dibasic Calcium Phosphate). USP 31 (Dibasic Calcium Phosphate Dihydrate).

Equivalence. Each g of calcium hydrogen phosphate (dihydrate) represents about 5.8 mmol of calcium and of phosphate. Calcium hydrogen phosphate (dihydrate) 4.29 g is equivalent to about 1 g of calcium.

### Calcium Lactate

Calcii lactas; Calcio, lactato de; Calcium, lactate de; E327; Kalcio laktatas: Kalciumlaktat: Kalcium-laktát: Kalsiumlaktaatti: Kalsivum Laktat; Mléčnan vápenatý; Wapnia mleczan. Calcium 2-hydroxypropionate.

 $C_6H_{10}CaO_6, xH_2O = 218.2$  (anhydrous); 308.3 (pentahy-

drate); 272.3 (trihydrate). CAS — 814-80-2 (anhydrous calcium lactate); 41372-22-9 (hydrated calcium lactate); 5743-47-5 (calcium lactate pentahydrate); 63690-56-2 (calcium lactate pentahydrate).

ATC - A 1 2AA05.

ATC Vet - QA I 2AA05.

Pharmacopoeias. In Chin., Eur. (see p.vii), Jpn, and US.

Eur. has separate monographs for the anhydrous substance, the monohydrate, the pentahydrate, and the trihydrate. US allows anhydrous or hydrous forms. Viet. has monographs for the pentahydrate and the trihydrate.

Ph. Eur. 6.2 (Calcium Lactate, Anhydrous; Calcii Lactas Anhydricus). A white or almost white, crystalline or granular powder. Soluble in water; freely soluble in boiling water; very slightly soluble in alcohol

Ph. Eur. 6.2 (Calcium Lactate Monohydrate: Calcii Lactas Monohydricus). A white or almost white, crystalline or granular powder. Soluble in water; freely soluble in boiling water; very slightly soluble in alcohol.

Ph. Eur. 6.2 (Calcium Lactate Pentahydrate; Calcii Lactas Pentahydricus). A white or almost white, slightly efflorescent, crystalline or granular powder. Soluble in water; freely soluble in boiling water; very slightly soluble in alcohol.

The BP 2008 gives Calcium Lactate as an approved synonym. Ph. Eur. 6.2 (Calcium Lactate Trihydrate; Calcii Lactas Trihydricus). A white or almost white, crystalline or granular powder. Soluble in water; freely soluble in boiling water; very slightly

USP 31 (Calcium Lactate). White, practically odourless, granules or powder. The pentahydrate is somewhat efflorescent and at 120° becomes anhydrous. The pentahydrate is soluble 1 in 20 of water and practically insoluble in alcohol. Store in airtight

Equivalence. Each g of calcium lactate (trihydrate) represents about 3.7 mmol of calcium. Each g of calcium lactate (pentahydrate) represents about 3.2 mmol of calcium. Calcium lactate (pentahydrate) 7.7 g and calcium lactate (trihydrate) 6.8 g are each equivalent to about 1 g of calcium.

# Calcium Lactate Gluconate

Calcio, gluconato lactato de.  $Ca_5(C_3H_5O_3)_6$ ,  $(C_6H_{11}O_7)_4$ ,  $2H_2O = 1551.4$ . ATC - A12AA06. ATC Vet — QA I 2AA06.

**Equivalence.** Each g of calcium lactate gluconate (dihydrate) represents about 3.2 mmol of calcium. Calcium lactate gluconate (dihydrate) 7.74 g is equivalent to about 1 g of calcium.

#### Calcium Lactobionate

Calcii Lactobionas: Calcio, lactobionato de: Calcium Lactobionate Dihydrate; Kalciumlaktobionat; Kalsiumlaktobionaatti. Calcium 4-0-β-D-galactopyranosyl-D-gluconate dihydrate.  $C_{24}H_{42}CaO_{24},2H_2O = 790.7.$ CÁS — 110638-68-1.

Pharmacopoeias. In US.

USP 31 (Calcium Lactobionate). pH of a 5% solution in water is between 5.4 and 7.4.

Equivalence. Each g of calcium lactobionate (dihydrate) represents about 1.3 mmol of calcium. Calcium lactobionate (dihydrate) 19.7 g is equivalent to about 1 g of calcium.

#### Calcium Levulinate (BAN)

Calcii Laevulas; Calcii laevulinas; Calcii Laevulinas Dihydricus; Calcii Levulinas Dihydricum; Calcio, levulinato de; Calcium Laevulate; Calcium Laevulinate; Calcium, lévulinate de; Kalcio levulinatas; Ka-Iciumlevulat; Kalcium-levulát dihydrát; Kalciumlevulinat; Kalciumlevulinát; Kalsiumlevulaatti; Kalsiumlevulinaatti; Lévulinate Calcique. Calcium 4-oxovalerate dihydrate.

 $C_{10}^{\dagger}H_{14}CaO_{6}, 2H_{2}O = 306.3.$ 

CAS — 591-64-0 (anhydrous calci 49-7 (calcium levulinate dihydrate). ATC — A12AA30. 591-64-0 (anhydrous calcium levulinate); 5743-

ATC Vet - QA I 2AA30.

**Pharmacopoeias.** In *Eur.* (see p.vii) and *US*.

Ph. Eur. 6.2 (Calcium Levulinate Dihydrate). A white or almost white, crystalline powder. Freely soluble in water; very slightly soluble in alcohol; practically insoluble in dichloromethane. A 10% solution in water has a pH of 6.8 to 7.8. Protect from light. USP 31 (Calcium Levulinate). A white crystalline or amorphous powder, having a faint odour suggestive of burnt sugar. Freely soluble in water; slightly soluble in alcohol; insoluble in chloroform and in ether. pH of a 10% solution in water is between 7.0 and 8.5.

Equivalence. Each g of calcium levulinate (dihydrate) represents about 3.3 mmol of calcium. Calcium levulinate (dihydrate) 7.64 g is equivalent to about 1 g of calcium.

### **Calcium Phosphate**

Calcii Phosphas; Calcio, fosfato de; Calcium Orthophosphate; E341; Fosfato Tricalcico; Fosforečnan vápenatý; Kalcio fosfatas; Kalcium-foszfát; Phosphate Tertiaire de Calcium; Phosphate tricalcique; Precipitated Calcium Phosphate; Tricalcii phosphas; Tricalcium Phosphate; Trikalciumfosfat; Trikalsiumfosfaatti; Wapnia fosforan.

CAS — 7758-87-4 (tricalcium diorthophosphate); 12167-74-7 (calcium hydroxide phosphate). ATC — A12AA01.

ATC Vet — QA12AA01.

**Description.** Calcium phosphate is not a clearly defined chemical entity but is a mixture of calcium phosphates that has been most frequently described as either tricalcium diorthophosphate,  $Ca_3(PO_4)_2 = 310.2$ , or  $Ca_5OH(PO_4)_3 = 502.3$ . calcium hydroxide phosphate, or

Pharmacopoeias. In Eur. (see p.vii), Int., and Viet. Also in US-

Ph. Eur. 6.2 (Calcium Phosphate) It consists of a mixture of calcium phosphates and contains 35 to 40% of Ca. A white or almost white powder. Practically insoluble in water; dissolves in dilute hydrochloric acid and in dilute nitric acid.

The BP 2008 gives Tribasic Calcium Phosphate as an approved

**USNF 26** (Tribasic Calcium Phosphate). It consists of a variable mixture of calcium phosphates having the approximate composition 10CaO.3P2O5.H2O. It contains not less than 34% and not more than 40% of calcium. A white, odourless, powder. Practically insoluble in water; insoluble in alcohol; readily soluble in 3N hydrochloric acid and in 2N nitric acid.

### Calcium Pidolate (pINNM)

Calcii Pidolas; Calcium Pyroglutamate; Pidolate de Calcium; Pidolato de calcio. Calcium 5-oxopyrrolidine-2-carboxylate. Кальций Пидолат

 $Ca(C_5H_6NO_3)_2 = 296.3.$ 

CAS — 31377-05-6.

Equivalence. Each g of calcium pidolate (anhydrous) represents about 3.4 mmol of calcium. Calcium pidolate (anhydrous) 7.39 g is equivalent to about 1 g of calcium.

### Calcium Silicate

Calcio, silicato de; E552.

CAS — 1344-95-2; 10101-39-0 (calcium metasilicate); 10034-77-2 (calcium diorthosilicate); 12168-85-3 (calcium trisilicate) ATC — A02ÁC02. ATC Vet - QA02AC02.

**Description.** A naturally occurring mineral, the most common forms being calcium metasilicate ( $CaSiO_3 = 116.2$ ), calcium diorthosilicate ( $Ca_2SiO_4 = 172.2$ ), and calcium trisilicate  $(Ca_3SiO_5 = 228.3)$ . It is usually found in hydrated forms containing various amounts of water of crystallisation. Commercial calcium silicate is prepared synthetically.

Pharmacopoeias. In USNF.

USNF 26 (Calcium Silicate). Crystalline or amorphous calcium silicate is a compound of calcium oxide and silicon dioxide containing not less than 4% of CaO and not less than 35% of SiO<sub>2</sub>. A white to off-white free-flowing powder. Insoluble in water; with mineral acids it forms a gel. A 5% aqueous suspension has a pH of 8.4 to 11.2.

### Calcium Sodium Lactate

Calcio, lactato sódico de.  $2C_3H_5NaO_3$ ,  $(C_3H_5O_3)_2Ca$ ,  $4H_2O = 514.4$ .

**Equivalence.** Each g of calcium sodium lactate (tetrahydrate) represents about 1.9 mmol of calcium and 3.9 mmol of sodium and of lactate. Calcium sodium lactate (tetrahydrate) 12.8 g is equivalent to about 1 g of calcium.

# **Adverse Effects and Treatment**

Oral calcium salts can cause gastrointestinal irritation; calcium chloride is generally considered to be the most irritant of the commonly used calcium salts.

Injection of calcium salts can also produce irritation, and intramuscular or subcutaneous injection in particular can cause local reactions including sloughing or necrosis of the skin; solutions of calcium chloride are extremely irritant and should not be injected intramuscularly or subcutaneously. Soft-tissue calcification has followed the use of calcium salts parenterally.

Excessive amounts of calcium salts may lead to hypercalcaemia. This complication is usually associated with parenteral use, but can occur after oral dosage, usually in patients with renal failure or who are also taking vitamin D. Symptoms of hypercalcaemia include anorexia, nausea, vomiting, constipation, abdominal pain, muscle weakness, mental disturbances, polydipsia, polyuria, nephrocalcinosis, renal calculi, and, in severe cases, cardiac arrhythmias and coma. Too rapid intravenous injection of calcium salts may also lead to symptoms of hypercalcaemia, as well as a chalky taste, hot flushes, and peripheral vasodilatation. Mild asymptomatic hypercalcaemia will usually resolve if calcium and other contributory drugs such as vitamin D are stopped (see also Vitamin D-mediated Hypercalcaemia, p.1668). If hypercalcaemia is severe, urgent treatment is required as outlined on p.1668.

### **Precautions**

Solutions of calcium salts, particularly calcium chloride, are irritant, and care should be taken to prevent extravasation during intravenous injection. Calcium salts should be given cautiously to patients with renal impairment, or diseases associated with hypercalcaemia such as sarcoidosis and some malignancies. In

addition, they should generally be avoided in patients with calcium renal calculi, or a history of renal calculi. Calcium chloride, because of its acidifying nature, is unsuitable for the treatment of hypocalcaemia caused by renal insufficiency or in patients with respiratory acidosis or failure.

Plasma-calcium concentrations should be monitored closely in patients with renal impairment and during parenteral dosage and if large doses of vitamin D are used concurrently.

### Interactions

Hypercalcaemia has occurred when calcium salts are given with thiazide diuretics or vitamin D. Vitamin D increases the gastrointestinal absorption of calcium and thiazide diuretics decrease its urinary excretion. Plasma-calcium concentrations should be monitored in patients receiving the drugs together.

Bran decreases the gastrointestinal absorption of calcium, and may therefore decrease the efficacy of calcium supplements. Corticosteroids also reduce calcium absorption.

Calcium enhances the effects of digitalis glycosides on the heart and may precipitate digitalis intoxication; parenteral calcium therapy is best avoided in patients receiving cardiac glycosides. Citrate salts increase the absorption of aluminium from the gastrointestinal tract (see Toxicity, under Adverse Effects of Aluminium Hydroxide, p.1706), therefore patients with renal failure taking aluminium compounds should avoid taking calcium citrate. Calcium salts reduce the absorption of a number of other drugs such as bisphosphonates, fluoride, some fluoroquinolones, and tetracyclines; doses should be separated by at least 3 hours.

### **Pharmacokinetics**

Calcium is absorbed mainly from the small intestine by active transport and passive diffusion. About one-third of ingested calcium is absorbed although this can vary depending upon dietary factors and the state of the small intestine; also absorption is increased in calcium deficiency and during periods of high physiological requirement such as during childhood or pregnancy and lactation. 1,25-Dihydroxycholecalciferol (calcitriol), a metabolite of vitamin D, enhances the active phase of absorption.

Excess calcium is mainly excreted renally. Unabsorbed calcium is eliminated in the faeces, together with that secreted in the bile and pancreatic juice. Minor amounts are lost in the sweat, skin, hair, and nails. Calcium crosses the placenta and is distributed into breast milk.

## **Human Requirements**

Calcium is the most abundant mineral in the body and is an essential body electrolyte. However, defining individual calcium requirements has proved difficult and guidelines vary widely by country and culture. Some authorities have adopted a factorial approach. For example, in the UK the dietary reference value (DRV) represents the apparent calcium requirements of healthy people under the prevailing dietary circumstances. The amount of calcium absorbed varies according to several factors including the requirements of the body, but is normally only about 30 to 40% of the dietary intake.

The richest dietary sources of calcium are milk and milk products. Significant amounts can also be consumed in green leafy vegetables, fortified flour, the soft bones of fish, and hard water.

**UK** and **US** recommended dietary intake. In the UK dietary reference values (DRV—see Human Requirements, p.1925) have been published for calcium. <sup>1</sup> In the USA recommended dietary allowances (RDA) had been set, <sup>2</sup> but have been replaced by dietary reference intakes (see p.1925). <sup>3</sup> In the UK the estimated average requirement (EAR) for adults is 525 mg (13.1 mmol) daily and the reference nutrient intake (RNI) for adults is 700 mg (17.5 mmol) daily; these figures are based on a mean absorption of calcium of 30% from mixed diets. In the USA the traditional RDA was 800 mg daily for adults aged over 25 years; this figure

Table 1. Some calcium salts and their calcium content.

	Calcium content per g		
Calcium salt	mg	mmol	mEq
Calcium acetate (anhydrous)	253	6.3	12.6
Calcium carbonate	400	10.0	20.0
Calcium chloride (dihydrate)	273	6.8	13.6
Calcium chloride (hexahydrate)	183	4.6	9.1
Calcium citrate (tetrahydrate)	211	5.3	10.5
Calcium glubionate (monohydrate)	66	1.6	3.3
Calcium glucoheptonate (anhydrous)	82	2.0	4.1
Calcium gluconate (monohydrate)	89	2.2	4.5
Calcium glycerophosphate (anhydrous)	191	4.8	9.5
Calcium hydrogen phosphate (dihydrate)	233	5.8	11.6
Calcium lactate (anhydrous)	184	4.6	9.2
Calcium lactate (trihydrate)	147	3.7	7.3
Calcium lactate (pentahydrate)	130	3.2	6.5
Calcium lactate gluconate (dihydrate)	129	3.2	6.4
Calcium lactobionate (dihydrate)	51	1.3	2.5
Calcium levulinate (dihydrate)	131	3.3	6.5
Calcium phosphate [10CaO.3P <sub>2</sub> O <sub>5</sub> .H <sub>2</sub> O]	399	10.0	19.9
Calcium pidolate (anhydrous)	135	3.4	6.7
Calcium silicate [CaSiO <sub>3</sub> ]	345	8.6	17.2
Calcium sodium lactate (tetrahydrate)	78	1.9	3.9

was based on an absorption rate of 40%. Under the new dietary reference intakes, adequate intakes (AI) for calcium have been set, which are higher in some age groups than the previous RDAs.  $^3$  For adults aged up to 50 years the AI is 1 g daily, and for those 51 years or older, it is 1.2 g daily.  $^3$  The tolerable upper intake is considered to be 2.5 g daily.  $^3$ 

- DoH. Dietary reference values for food energy and nutrients for the United Kingdom: report of the panel on dietary reference values of the committee on medical aspects of food policy. Report on health and social subjects 41. London: HMSO, 1991.
- Subcommittee on the tenth edition of the RDAs, Food and Nutrition Board, Commission on Life Sciences, National Research Council. Recommended dietary allowances. 10th ed. Washington, DC: National Academy Press, 1989. Also available at: http://www.nap.edu/openbook.php?isbn=0309046335 (accessed 21/07/08).
- Standing Committee on the Scientific Evaluation of Dietary Reference ence Intakes of the Food and Nutrition Board. Dietary Reference Intakes for calcium, phosphorus, angnesium, vitamin D, and fluoride. Washington, DC: National Academy Press, 1999. Also available at: http://www.nap.edu/openbook.php?isbn=0309063307 (accessed 21/07/08)

### **Uses and Administration**

Calcium salts are used in the management of **hypocal-caemia** (p.1668) and **calcium deficiency states** resulting from dietary deficiency or ageing (see also Osteoporosis, p.1084). Doses may be expressed in terms of mmol or mEq of calcium, mass (mg) of calcium, or mass of calcium salt (for comparative purposes, see Table 1, above).

In simple deficiency states calcium salts may be given orally, usually in doses of 10 to 50 mmol (400 mg to 2 g) of calcium daily adjusted to the individual patient's requirements.

In severe acute hypocalcaemia or hypocalcaemic tetany parenteral dosage is necessary, generally by slow intravenous injection or continuous infusion of calcium chloride or calcium gluconate (see also Administration, below). A typical dose is 2.25 to 4.5 mmol of calcium by slow intravenous injection, either repeated as required, or followed by continuous intravenous infusion of about 9 mmol daily. 2.25 mmol of calcium is provided by 10 mL of calcium gluconate 10%. Calcium gluceptate and calcium glycerophosphate with calcium lactate have been given by the intramuscular route; the chloride and gluconate are unsuitable for this route because of their irritancy. The intravenous route is used in children.

Intravenous calcium salts are also used to reverse the toxic cardiac effects of potassium in the emergency

treatment of severe **hyperkalaemia** (p.1669), and as an antidote to magnesium in severe **hypermagnesaemia** (p.1668). For these indications, 2.25 to 4.5 mmol of calcium (10 to 20 mL of calcium gluconate 10%) is commonly used.

Individual calcium salts have specific uses. Calcium carbonate (p.1714) or acetate are effective phosphate binders and are given orally to reduce phosphate absorption from the gut in patients with **hyperphosphataemia**; this is particularly relevant to patients with chronic renal failure in order to prevent the development of renal osteodystrophy (p.1086). The initial dose of calcium carbonate is 2.5 g daily titrated to a maximum of 17 g daily. A typical initial dose of calcium acetate is 3 or 4 g daily; most patients require 6 to 12 g daily.

Calcium carbonate and calcium silicate, given orally, are used for their **antacid** properties (p.1692).

Some of the calcium salts discussed here also have *pharmaceutical uses* as diluents in capsules and tablets, buffers and dissolution aids in dispersible tablets, disintegrant and anticaking agents, and as a basis or abrasive in dental preparations. Calcium phosphate is also used as a bone graft substitute.

**Homoeopathy.** Various calcium salts have been used in homoeopathic medicines under the following names:

- · Calcium acetate: Calcarea acetica; Calc. ace.
- Calcium arsenite: Calcium arsenicosum; Calcarea arsenicosa; Cal. ars.
- · Calcium chloride: Calcarea muriatica; Cal. mur.
- Calcium hydrogen phosphate: Calcium phosphoricum
- Calcium hypophosphite: Calcarea hypophosphorosa; Calc. hyp.
- Calcium oxalate: Calcarea oxalica; Cal. oxal.
- Calcium phosphate: Calcarea phosphorica; Calc. phos.; Cal. phos.
- · Calcium picrate: Calcarea picrata; Cal. pic.
- Calcium silicate: Calcarea silicata; Calc. sil.

Other calcium salts used in homoeopathy and described elsewhere include: calcium bromide (p.2269), calcium carbonate (p.1714), calcium fluoride (p.1932), calcium hydroxide (p.2272), calcium iodide (p.1553), and calcium sulfate (p.2273).

Administration. Some prefer calcium chloride to calcium gluconate for parenteral preparations, <sup>1,2</sup> because retention of the chloride is greater and more predictable than of the gluconate, and results in a more predictable increase in extracellular ionised calcium concentration. However, calcium chloride is considered to be the most irritant of the calcium salts in general use (see Adverse Effects, above).

Calcium gluconate has been given by the intraperitoneal route<sup>3</sup> for the treatment of chronic hypocalcaemia after parathyroidectomy in a patient undergoing continuous ambulatory peritoneal dialysis, resulting in improved systemic bioavailability compared with oral and intravenous use.

- Worthley LIG, Phillips PJ. Intravenous calcium salts. Lancet 1980; ii: 149.
- Broner CW, et al. A prospective, randomized, double-blind comparison of calcium chloride and calcium gluconate therapies for hypocalcemia in critically ill children. J Pediatr 1990; 117: 986-9.
- Stamatakis MK, Seth SK. Treatment of chronic hypocalcemia with intraperitoneal calcium. Am J Health-Syst Pharm 1995; 52: 201–3.

**Bites and stings.** Calcium gluconate 10% solution has been given intravenously as an alternative to the use of conventional muscle relaxants for the management of pain and muscle spasm associated with neurotoxic spider envenomation (p.2239) by species such as *Latrodectus mactans* (black widow spider). <sup>1,2</sup> Although the precise mechanism of action of calcium in the alleviation of neuromuscular symptoms is unknown it is believed to be due to the replenishment of calcium stores in the sarcoplasmic reticulum of muscle depleted by stimulation.

- Binder LS. Acute arthropod envenomation: incidence, clinical features and management. *Med Toxicol Adverse Drug Exp* 1989; 4: 163–73.
- Woestman R, et al. The black widow: is she deadly to children? Pediatr Emerg Care 1996; 12: 360–4.

**Bone disease.** Calcium is essential for the development and maintenance of normal bone, and calcium salts may be indicated in the treatment of some bone disorders associated with calcium

deficiency, such as certain types of osteomalacia and rickets (p.1084). Oral doses of 1 to 3 g of calcium daily are used in osteomalacia

Oral calcium supplements can also be used as an adjunct in the management of osteoporosis (p.1084) and corticosteroid-induced osteoporosis (see Effects on Bones and Joints, under Corticosteroids, p.1491).

Cramps. Calcium salts are one of a number of interventions that have been tried in the management of cramps (see Muscle Spasm, p.1887). However, evidence for these interventions is mostly lacking and a small systematic review concluded that oral calcium was not of benefit for leg cramps during pregnancy.

1. Young GL, Jewell D. Interventions for leg cramps in pregnancy Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2002 (accessed 21/06/05).

Diagnosis of insulinoma. Calcium stimulates the release of insulin from insulinomas. Intra-arterial calcium gluconate, followed by hepatic venous sampling, has been found to be accurate and sensitive in the diagnosis and localisation of insulinomas,  $^{1.4}$ even when other investigations have been negative.5,

- 1. Doppman JL, et al. Localization of insulinomas to regions of the pancreas by intra-arterial stimulation with calcium. Ann Intern Med 1995; 123: 269-73.
- 2. Lo CY, et al. Value of intra-arterial calcium stimulated venous sampling for regionalization of pancreatic insulinomas. *Surgery* 2000; **128**: 903–9.
- 3. Brändle M, et al. Assessment of selective arterial calcium stimulation and hepatic venous sampling to localize insulin-secreting tumours. *Clin Endocrinol (Oxf)* 2001; **55:** 357–62.
- 4. Grant CS. Insulinoma. Best Pract Res Clin Gastroenterol 2005;
- 5. O'Shea D, et al. Localization of insulinomas by selective intraar terial calcium injection. J Clin Endocrinol Metab 1996; 81:
- 6. Pereira PL, et al. Insulinoma and islet cell hyperplasia: value of the calcium intraarterial stimulation test when findings of other preoperative studies are negative. Radiology 1998; 206: 703-9.

Fluoride toxicity. Inorganic fluoride is corrosive to skin and mucous membranes and acute intoxication disrupts many physiological systems; severe burns and profound hypocalcaemia may ensue. Absorption of the fluoride can be prevented by conversion to an insoluble form such as calcium fluoride and thus irrigation of skin (or gastric lavage as appropriate) with lime water, milk, or a 1% solution of calcium gluconate is recommended. Immediate treatment should also consist of 10 mL of calcium gluconate 10% intravenously, repeated after one hour; 30 mL should be given if tetany is present. In the short term affected skin and tissue should be injected with a 10% solution of calcium gluconate at a dose of 0.5 mL/cm<sup>2</sup> and burnt skin treated with a calcium gluconate 2.5% gel.1

See also under Hydrofluoric Acid, p.2322.

McIvor ME. Acute fluoride toxicity: pathophysiology and management. Drug Safety 1990; 5: 79–85.

Hypertension. Meta-analysis suggests that calcium supplementation results in a small reduction in systolic and diastolic blood pressure. 1 Although the effect was too small to support the use of calcium supplementation for preventing or treating hypertension (p.1171), it is possible that calcium supplementation might have beneficial effects on blood pressure in those with an inadequate intake. In a controlled trial, calcium with vitamin D supplementation reduced systolic blood pressure more effectively than calcium alone.2

- 1. Griffith LE. et al. The influence of dietary and nondietary calcium supplementation on blood pressure: an updated metaanalysis of randomized controlled trials. *Am J Hypertens* 1999; **12**: 84-92
- 2. Pfeifer M. et al. Effects of a short-term vitamin D and calcium supplementation on blood pressure and parathyroid hormone levels in elderly women. *J Clin Endocrinol Metab* 2001; **86:**

PREGNANCY. Despite an earlier meta-analysis1 which concluded that calcium supplementation during pregnancy reduced systolic and diastolic blood pressure and the incidence of preeclampsia and hypertension, results from a double-blind, placebo-controlled trial in a total of 4589 women indicated that calcium supplementation during normal pregnancy did not prevent pre-eclampsia, pregnancy-associated hypertension without pre-eclampsia, or a number of other related disorders.2 A subsequent review3 found that calcium supplementation was beneficial, but it was noted that there was a wide variation in results between different studies; most of the effect was in studies including women identified as being at high risk for pre-eclampsia, and results from studies including lower-risk women found that calcium had no effect. The highrisk studies were carried out in areas with a low dietary calcium intake, suggesting that benefit might be greatest in such populations. However, a further study in 8325 women living in areas with a low calcium intake but not specifically at high risk found that calcium supplementation had no significant effect on the incidence of pre-eclampsia, although it did reduce the risk of severe pre-eclamptic complications. An updated meta-analysis,5 which included this study, concluded that calcium supplementation during pregnancy was safe and that it did reduce the incidence of pre-eclampsia and serious complications, particularly in high-risk women.

For discussions of hypertension in pregnancy and eclampsia and pre-eclampsia, see p.1171 and p.470, respectively.

- Bucher HC, et al. Effect of calcium supplementation on pregnancy-induced hypertension and preeclampsia: a meta-analysis of randomized controlled trials. *JAMA* 1996; **275**: 1113–17. Correction. *ibid.*; **276**: 1388.
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Malignant neoplasms. There is some evidence that calcium supplementation may modestly reduce the risk<sup>1-3</sup> of colorectal cancer and its recurrence. 4-6 This protective effect appears to be more pronounced for advanced colorectal lesions, and when serum concentrations of vitamin D are in the higher range.8

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- 3. Cho E, et al. Dairy foods, calcium, and colorectal cancer: a pooled analysis of 10 cohort studies. J Natl Cancer Inst 2004; 96: 1015-22. Correction. ibid.: 1724.
- 4. Baron JA, et al. Calcium supplements for the prevention of
- colorectal adenomas. N Engl J Med 1999; **340:** 101–7. 5. Bonithon-Kopp C, et al. Calcium and fibre supplementation in prevention of colorectal adenoma recurrence; a randomised inervention trial. Lancet 2000; 356: 1300-6.
- 6. Martínez ME, et al. Calcium, vitamin D, and risk of adenoma recurrence (United States). Cancer Causes Control 2002; 13: 213–20.
- 7. Wallace K, et al. Effect of calcium supplementation on the risk of large bowel polyps. J Natl Cancer Inst 2004; 96: 921-5
- 8. Grau MV, et al. Vitamin D, calcium supplementation, and color-ectal adenomas: results of a randomized trial. J Natl Cancer Inst 2003: 95: 1765-71.

Premenstrual syndrome. Calcium supplementation was effective in relieving the luteal phase symptoms of premenstrual syndrome (p.2099) in 1 study. A review of this and other studies suggested that calcium supplementation at a dose of 1.2 to 1.6 g daily should be considered in patients with premenstrual syn-

- 1. Thys-Jacobs S, et al. Calcium carbonate and the premenstrual syndrome: effects on premenstrual and menstrual symptoms. Am J Obstet Gynecol 1998; 179: 444–52.
- 2. Ward MW, Holimon TD. Calcium treatment for premenstrual syndrome. Ann Pharmacother 1999; 33: 1356-8.

### **Preparations**

**BP 2008:** Calcium and Ergocalciferol Tablets; Calcium Chloride Injection; Calcium Gluconate Injection; Calcium Gluconate Tablets; Calcium Lactate Tablets; Effervescent Calcium Gluconate Tablets;

BPC 1973: Calcium with Vitamin D Tablets:

USP 31: Alluminum Sulfate and Calcium Acetate for Topical Solution; Aluminum Sulfate and Calcium Acetate Tablets for Topical Solution; Calcium Acetate Tablets; Calcium Chloride Injection; Calcium Glubionate Syrup; Calcium Gluceptate Injection; Calcium Gluconate Injection; Calcium Gluconate Tablets; Calcium Levulinate Injection; Calcium With Vitamin D Tablets; Dibasic Calcium Phosphate Tablets; Half-strength Lactated Ringer's and Dextrose Injection; Lactated Ringer's and Dextrose Injection; Lactated Ringer's Injection; Potassium Chloride in Lactated Ringer's Injection; Potassium Chloride Inj er's and Dextrose Injection.

### Proprietary Preparations (details are given in Part 3)

Arg.: Calcium-Sandoz; Citicum-Sandoz; Calcium-Sandoz; Calcium-Chile: Calcium-Sandoz; Phos-Ex; Fin.: Calcium-Sandoz; Osteocit; Chile: Calcium-Sandoz; Osteocit; Chile: Calcium-Sandoz; Phos-Ex; Fin.: Calcium-Sandoz; Phos Denm.: Calcium-Sandoz': Phos-Ex; Fin.: Calcium-Sandoz; Phos-Ex; Fr.: CAL Ocean; Calcium-Sandoz; Alcikidat'; Ostram; Gen.: Calciratt; Calcium Eifelfango†; Calcium Fresenius†; Calcium-Sandoz; Cerasorb; Eubiolac; Phos-Ex; Gr.: Neocalcitic Osteore; Nosteus; Hong Kong; Calcium-Inson; Calcium Vida; Calcium-Sandoz†; Citracal; Gluco-Calcium; Mega-Cal; Hung; Bano; Calcium-Sandoz†; Citracal; Cluco-Calcium; India: Calcium-Sandoz; Phosforid; Hodon.: Dumocalicn; Licokalk; Inl.: Calcium-Sandoz†; Sandocal; Israel: Calcium-Sandoz; Ital.: Calcetat; Calcium-Sandoz; Nadloysia: Ca Lac†; Citracal†; Trocium†; Mex.: Bionokaltran; Bon-Ker†; Calcidef. Calcidefox; Calcigenol Doble; Calciofem; Calcium-Sandoz; Calcival; Ostram†; Neth.: Calcium-Sandoz; Phos-Ex; Norw.: Calcium-Sandoz; Calcival; Calciv Ostram | Netri. Calcium-Sandoz | Philipp.: Calcebone; United Home Calactate; Pol.: Calcium-Sandoz | Philipp.: Calcebone; United Home Calactate; Pol.: Calcium Calfit; Calcium Syrop; Ostical; Ostram; Sanosvit Calcium; Sandoz Forte: Calcium-Sandoz Forte; (Kansuwi-Cara,oa Oopre); S.Afr.: Calcium-Sandoz, Glucal; Singopore: Calcium-Sandoz; Citracal; Hydrofluoric Acid Antidote†; Os-Cal; Vitacal; Spain: Calcio 20 Emulsion; Calcium-Sandoz; Forte; Calcium-Sandoz; Calc Sandoz†; Ibercal; Oseofort; Ostram; Royen; Tepox Cal; Swed.: Calcium-Sandoz; Phos-Ex; Switz.: Calcium-Sandoz; Thai.: Calcibon†; Calcium Unison; Calcium-Sandoz; Calsop; Calvin; Kal-Forte; Lo-P-Caps; Turk.: Anti-Fosfat Ca; Calcium-Sandoz; Phos-Ex; UK: BioCalth; Calcium-Sandoz; Ostram; Phos-Ex; Sandocal; **USA**: Cal-C; Cal-Citrate; Cal-G; Cal-Lac; Cal-phron; Citracal; Oyster Calcium; PhosLo; Posture; **Venez.**: Calcibon; Calcitrex; Calcium-Sandoz; Citracal; Maxical; Oscale.

Multi-ingredient: Arg.: Anartrit; Anusol-A; Beriplast P; Calcimax D3; Calcio Cit; Calcional D3; Calcium D†; Cavirox Cit; Citramar D; Flucalin; Isaflavon; Magnesio Incaico; Noacid Diates; Ostram D3; Regucal D; Sojar Plus-Calcio; Tissucol; Tissucol Duo Quick†; Austral: Bioglan Ciriflo†; Biog-

lan Mens Super Soy/Clover; Bioglan Soy Power Plus; Cardioplegia A; Celloid Compounds Magcal Plus; Celloid Compounds Sodical Plus; Chelated Caldag, Duo Celloids CPP, Duo Celloids CPPP; Duo Celloids CPPP; Duo Celloids PCCP; Duo Celloids SPCP; Estrafife Meno-Care; Extrafife Sleep-Care; FAB Tri-Cal; Magnesium Plus; PhytoLife; Forsteot; Silici Complex; Soy Forte with Black Cohosh†, Tisseel Duo; Tyroseng†; Austria: Beriplast; Calcipot C; Calcipot D: Calcisan; Calcisan B + C; Calcisan C; Calcisan D; Centramin; Coldargan; Coldistan; EST; Famel cum Codein; Famel cum Ephedrin; Lactolavo; Macahitt Maxi-Kalz; Mega-Calcium; Orocholin; Ruticalzon; Tissucol; Tissucol Duo Quick; Belgs; Sandoz Calcium + Vitamine C†; Tissucol Duo; Topcal Duo Quick; Belgs; Sandoz Calcium + Vitamine C†; Tissucol Duo; Topcal Dia; Brazz: Alergo Glucalbet†; Beriplast P; Calcifix B12; Calcifix Inradiado; Calcigenoi; Calcino Complexo; Calcium C; Calcium Sandoz + Vitamina C†; Calcium Child; Calcium; Tisseel; Chile; Beriplast P; C-1000-C†; Calcigran; Calcimax D3; Calcio 520; Calcio Cm; Calcio Nilf; Calciovit Puro; Calcium-Sandoz Forte D; Caprimida D Balance; Crevet Calcio + D3 + C; Elacl-D; Kaplus-D; Ostram D3; Trical-D; Tridin†; Cz.: Calcium C Neo; Calcium C†; Calcium-Sandoz FF; Calcium-Sandoz Forte; Methiaden Calcium†; OsvaRen; Tissucol; Tiorin, Denna: Tisseel Duo Quick; Fin.: D-Calcor; Mega-Calcium; Ostram-Vit D†; Tisseel Duo Quick; Fin.: D-Calcor; Galiron-C; Carbophos; Catariod†; Cohoro-Magnon; Cristopal†; Curaster; Desintex Infantile; Dops; Estrofort; Frubiose Vitamine D†; Galactogli; Galirenef; Gastropax; Ostram Vitamine D; Quixi; Pissuol; Vargostabit; Verruivse-Methionine; Gez:: Acidowerth: Berniast; \*\*Pr.: Bernplast; Ca-C-t; Calciforte; Carbophos; Catandolf; Chloro-Magnesion†; Ciristopal†; Curaster; Desintex Infantile; Dops; Estrofort; Trubiose Vitamine D†; Galactogii; Galirene†; Gastropax; Ostram Vitamine D; Quixil; Tissucol; Vagostabyl; Verrulyse-Methionine; Gerz: Acidovert; Beriplast; Calcipot; Calcium Braun; Calcium-dura Vit D; Calcium-Rutinion†; calcivitase†; Ermsech†; Ferno-C-Calcium; Fluoril; Frubiase Calcium forte 500; Frubiase Calcium T; Hicotorpi; Junisana†; Osscrvitin-A†; Ossofortin†; Osspulvit S forte†; Osspulvit S†; Quixil; rohasal†; Tissucol Duo S; Tissucol-Kit; Tindin; Grz: Beriplast P; Caldes†; Cidominet; Decel; Ravobion-C; Frubiose-N†; Gluta-calcium†; Iodocollyre; Mega-Calcium; Hong Kong: Beriplast P, Ca-C†; Callimon: Caltrate + D; Caltrate Plus; Citracal + D; Liverall†; Magesto; Mega-Cal with Vit D; Osteocare; Scott's Emulsion Orange; Tisseel; Tridin; Hung; Beriplast; P, Burofix†; Calciphednin†; Calcium-Sandoz + Vitamin C; Caldea†; Colclargan; Fagior†; Tissucol-Kit; Tirdin; Trypsin†; India: Alfacip Plus, Aristrol Forte†; Cadisper C; Cafe-Kit†; Calcinol; Catarest; Cato-Belt; CKP, Cotary; Gynae-CVP; Kalpastic; Kalzana; Macalvit; Milical; Milical; XP†; Omilcal; Ossivite; Ostebon; Ostocalcium; Ostocalcium B-12; Sigmacalvit; Siochrome; Styptocid; Styptocip†; Indon.: Beriplast; Cal-S; Calc-Os; Calcidin; Calcimega; Calcium Ad; Calcium-Sandoz; Calcium-Sandoz Forte; Calcium-Sandoz; Osimax; Ossovit; Osteocare; Osteopor; Oxcal; Scott's E Vita; Scott's Emulsion; Steopor; Davacalcium + D. + K. Bio: Calcium + D. + K. Bio: Calcium + D. + K. Bio: Calcium + D. + K. Plus Hi-Bone; jointfit; Laktafit; Licokalk Plus; Menoxa; Osimax; Ossovit; Oscocare; Osteopor; Oxcal; Scott's E Vita; Scott's Emulsion; Steopor; Thymcal; Totilac; Vosteon; Irl.: Bio-Calcium + D; Bio-Calcium + D + K; Caltrate Plus; Chocovite; Decal; Osteofos D3; Israel: Beriplast; Galcium Citrate; Calcium-Sandoz + Vit C; Quixij; Tisseel; Ital; Beriplast; Biotassina; Calcio Dobetin; Calciozim†; Calciumcafe; Calisvit; CalplusD3; Caltrate; Famel†; Foscald3; Ginvapast; Jodo Calcio Vitaminico, Katoxyn; Lactocol; Osseois Calcium; Ostram D; Ottofluor; Polijodurato; Quixil; Rex; Sedocalcio; Sedopuer F; Silvia Osteo; Tissucol; Tridin; Malaysia: Adult Catran Cal Man D3; Bio Estapaco Calcium; Blus Calcium; Sustam V. Vitania nex, secuciaio, peudopeir , india Seise), risascul, riiain, **mainysta:** Aictirex Cal-Mag-D3; Bio-Enhanced Calcium Plus; Calcium-Sandoz + Vitamin C; Calcium-Sandoz Forte†; Citracal + D†; Dumocalcin†; Junior Citrex Cal-Mag-D3; Milical; Supa Biocal Vitahealth†; **Mex.:** Bedoce-Cal; Beriplast P; C-Mag-D3; Milical; Supa Biocal Vitahealth†, Mex.: Bedoce-Cal: Beriplast P; С 1000-C: Calciyodina; Calpharma: Caltrec†; Domeboro; Emulsion de Scott; Fluoxyti; Osteocalcio; Posture D; Sandoz Calcium + D; Serracal; Tissucol†; Neth.: Beriplast P; Calisvit; Quixit; Tissucol†, Tissucol Duo; Philipp.: Caltrate Plus; Glutaphos; Her Soy Plus; Osteo-are; Time-Cee; Ton-A; Pol.: Ascalcin; Ascalcin Plus; Ascorutical; Beriplast; Calcium C; Sirupus Pini Com-positus; Sirupus Tussipini Sirupus Tussipini D; Wamag-Port. Bidiam; Ca-C; Calcigenol; Calcium 600†; Decalcit; Mucal†; Ostram D3†; Osvaren; Osvical; Quixil; Tissucol Duo; Rus.: Antigrippin-ANVI (Антигриппин-AHBIV); Cal-cemin (Кальцемин); Calcemin Advance (Кальцемин Адванс); S.Afr.: Phy-topause BSF; Sandoz Calcium-C†; Vitaplus C Plus; Singapore: BoneCare; Ca-C; Cavit-D3; Citrical + D; Dumocalcin; Flexzee†; Lacto Calcium†; Oscemin (Kansuemur): Calcemin Advance (Kansuemuri Agaarc): S. Afr.: Phytopause BSF: Sandoz Calcium-C; Vitaplus C Plus; Singopore: Bone Care; Ca-C; Cavit-D3; Citracal + D; Dumocalcin; Flexzee; Lacto Calcium†; Oscal + D; Vita Calmag Zn†; Vitacal; Vitacal + D; Spain: Alka-Seltzer; Beripast P Combis Boldolavini\*, Calcio 20 Guerte, Calcium-Sandoz Forte D; Creacal†; Duplicalcio 150†; Duplicalcio B12; Duplicalcio Hidraz†; Ginejuvent; Ibercal D; Mencalisvit; Metafisol; Osteomerck Osvical D; Tepox Cal D; Tissucol Duo; Trabex; Swed: Macalvit; Relavit; Tisseel Duo Quick; Switz.: Beriplast P; C-Calcium; Ca-C†; Calcium D Sauter; Calcivit; Callimon†; Calpred; Decalcit; Demostan N; Famel; Ingex; Cinvapast; Glucocalcium; Phytopharma Calcium; Pidocal†; Silex; Tissucol Tissucol Duo S; Vin Tonique de Val‡; Thai: Bio-Calcium + D3 + K; Biocalron; Ca-C; Cal-D-Vita; Calcalcin; Calchew; Calcioday-D†; Calcium D; Caltrate Plus; Calvin Plus; Combi-Cal†; Gluco-Calcium; Ostone-B12; Phocium†; Turk.: Beriplast P; Calcidne; Calcimax D3; Calcium Picken; Calcium-Sandoz C; Caltrate; Folic Plus; Fosfokalsyum; Fungecyi; Kalsifluor; Nature Made Oyster Shell Calcium; Ostocare; Tisseel VI; UK; Calcimax; Calcium and Ergocalciferol Tablets; Calcium Clear; Calfovit D3; Caltrate Plus; Crampex; Glykola; Haliborange Calcium Plus Vitamin D; Osteo-Life; Osteopro; Phytolife Plus; S.PH.P; Salivix; Tisseel; USA: Artiss; Bayer Womens Aspirin Plus Calcium; Bluboro†; Boropak†; Calcet; Calphosan; Caltrate Plus; Calvine D1; Pacifical Creamy Bites†; Citracal Plus with Magnesium; Domeboro; Ester-C Plus; GEM 215; Mag-Cal Mega Magonate; Oyster Calcium with Vitamin D; Pedi-Boro Soak Ras; Posture-D; PremesisRy Venez.: A-D-Vit; Calcibon D; Calcibon D Magnesio; Calcibon D Soya; Calcibon Natal; Calcinor D; Calciofar D; Calciogenol; Calcion D Plus; Calcitrex D3; Calpal D†; Citracal D; Dicalcico†; Gestocal†; Maltocalcine.

Used as an adjunct in: Swed.: Deltison.

## Magnesium

Magnesio; Magnésium; Magnez. Mg = 24.305.

Description. Magnesium is a cation given as various magnesium-containing salts.

Incompatibility. Magnesium salts have been reported to be incompatible with a wide range of drugs.

## Magnesium Acetate

Magnesii acetas tetrahydricus; Magnesio, acetato de; Magnésium (acétate de) tétrahydraté; Magnesiumacetattetrahydrat; Magnesiumasetaattitetrahydraatti; Magnézium acetáttetrahidrát; Magnezu octan; Magnio acetatas tetrahidratas; Octan hořečnatý tetrahvdrát.

 $C_4H_6MgO_4, 4H_2O = 214.5$ . CAS — 142-72-3 (anhydrous magnesium acetate); 16674-78-5 (magnesium acetate tetrahydrate).