Calcium Carbonate

1 Nonproprietary Names

BP: Calcium carbonate
JP: Precipitated calcium carbonate
PhEur: Calcii carbonas
USP: Calcium carbonate

2 Synonyms

Barcroft; *Cal-Carb*; *CalciPure*; calcium carbonate (1 : 1); creta preparada; *Destab*; E170; *MagGran CC*; *Millicarb*; *Pharma-Carb*; *Precarb*; precipitated carbonate of lime; precipitated chalk; *Sturcal*; *Vivapress Ca*.

3 Chemical Name and CAS Registry Number

Carbonic acid, calcium salt (1 : 1) [471-34-1]

4 Empirical Formula and Molecular Weight

$CaCO_3$

100.09

5 Structural Formula

$CaCO_3$

6 Functional Category

Tablet and capsule diluent; therapeutic agent.

7 Applications in Pharmaceutical Formulation or Technology

Calcium carbonate, employed as a pharmaceutical excipient, is mainly used in solid-dosage forms as a diluent.[1–3] It is also used as a base for medicated dental preparations, and as a buffering and dissolution aid in dispersible tablets.[4] Calcium carbonate is used as a bulking agent in tablet sugar-coating processes and as an opacifier in tablet film-coating.[5]

Calcium carbonate is also used as a food additive and therapeutically as an antacid and calcium supplement.[6]

8 Description

Calcium carbonate occurs as an odorless and tasteless white powder or crystals.

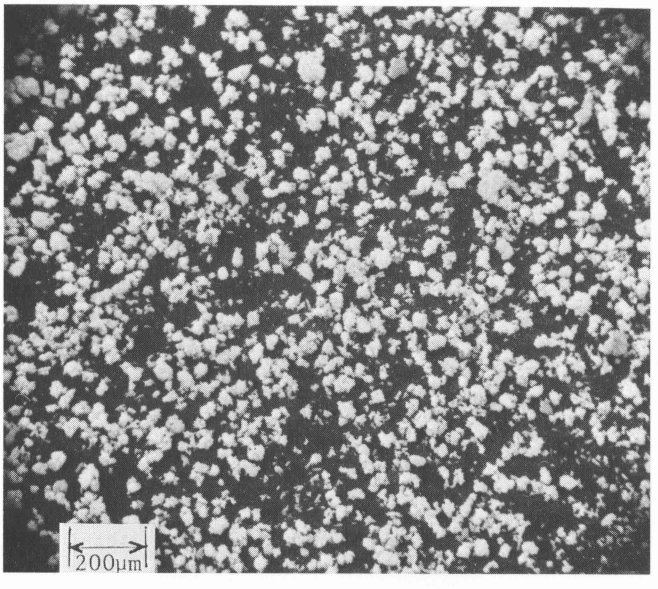
9 Pharmacopeial Specifications

See Table I.

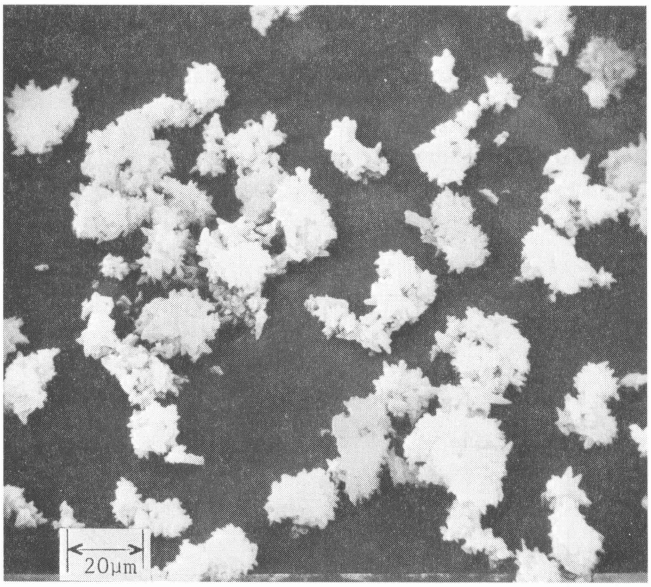
Table I: Pharmacopeial specifications for calcium carbonate.

Test	JP 2001	PhEur 2002	USP 25
Identification	+	+	+
Characters	—	+	—
Loss on drying	⩽1.0%	⩽2.0%	⩽2.0%
Acid-insoluble substances	⩽0.2%	+	⩽0.2%
Substances insoluble in acetic acid	—	⩽0.2%	—
Fluoride	—	—	⩽0.005%
Arsenic	⩽5 ppm	⩽4 ppm	⩽3 ppm
Barium	+	+	+
Chlorides	—	⩽330 ppm	—
Lead	—	—	⩽3 ppm
Iron	—	⩽200 ppm	⩽0.1%
Heavy metals	⩽20 ppm	⩽20 ppm	⩽0.002%
Magnesium and alkali (metals) salts	⩽0.5%	⩽1.5%	⩽1.0%
Sulfates	—	⩽0.25%	—
Mercury	—	—	⩽0.5 ppm
Organic volatile impurities	—	—	+
Assay (dried basis)	⩾ 98.5%	98.5%–100.5%	98.0%–100.5%

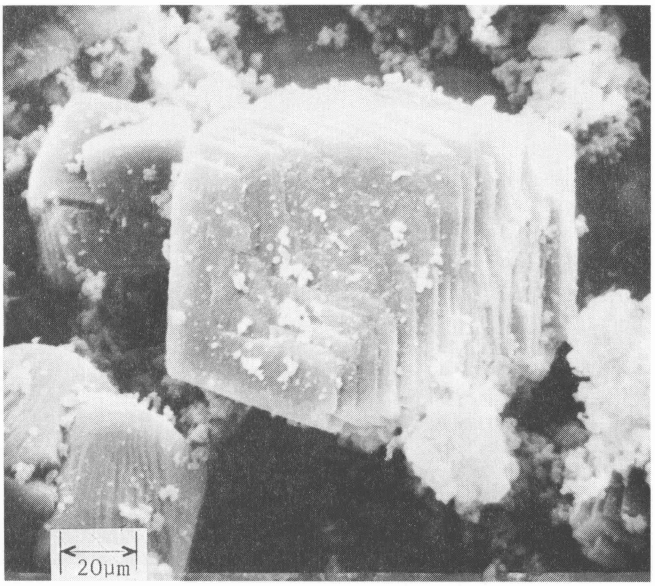
SEM: 1
Excipient: Calcium carbonate
Manufacturer: Whittaker, Clark & Daniels
Lot No.: 15A-3
Magnification: 600×
Voltage: 20 kV



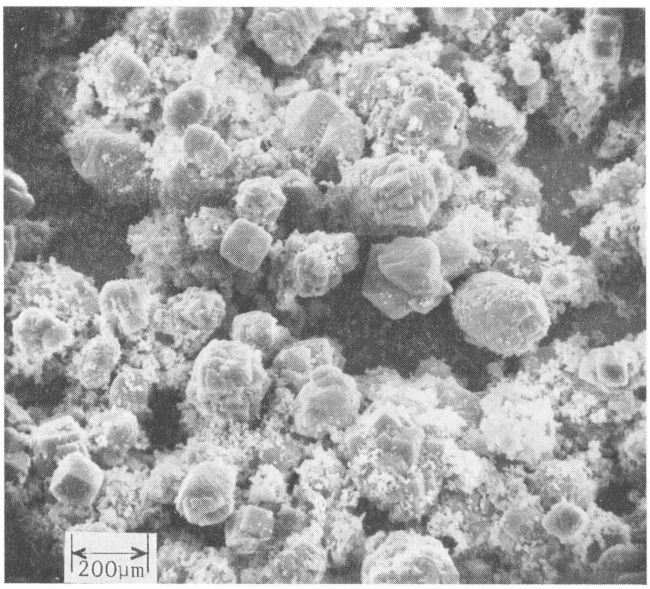
SEM: 2
Excipient: Calcium carbonate
Manufacturer: Whittaker, Clark & Daniels
Lot No.: 15A-3
Magnification: 2400×
Voltage: 20 kV



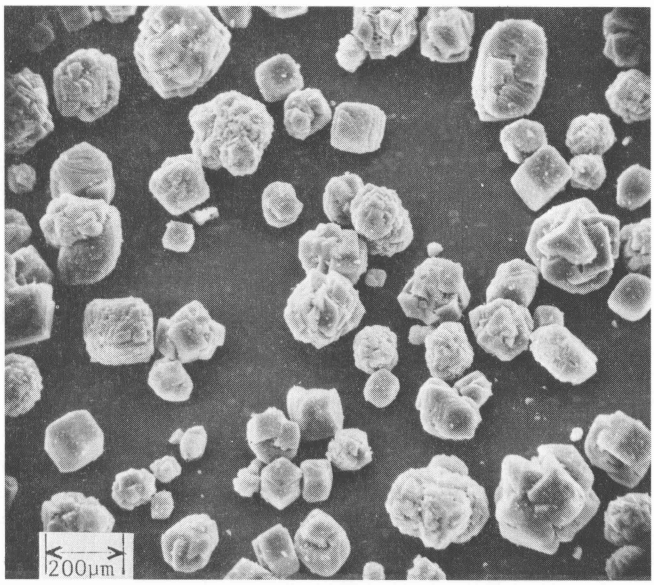
SEM: 4
Excipient: Calcium carbonate
Manufacturer: Whittaker, Clark & Daniels
Lot No.: 15A-4
Magnification: 2400×
Voltage: 20 kV



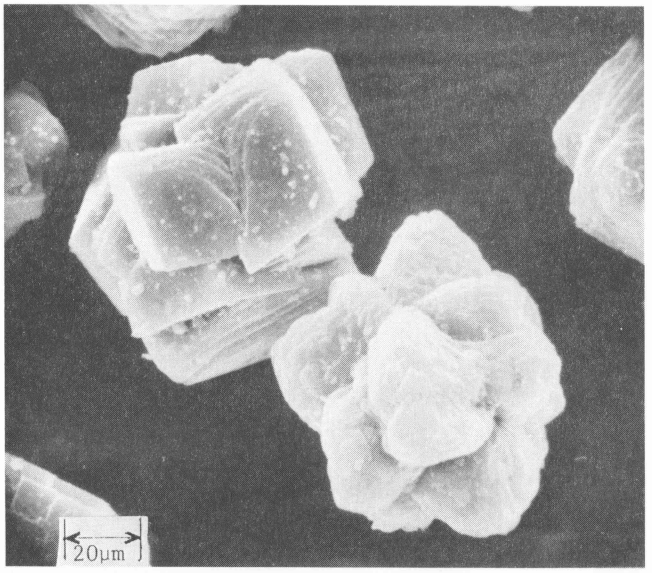
SEM: 3
Excipient: Calcium carbonate
Manufacturer: Whittaker, Clark & Daniels
Lot No.: 15A-4
Magnification: 600×
Voltage: 20 kV



SEM: 5
Excipient: Calcium carbonate
Manufacturer: Whittaker, Clark & Daniels
Lot No.: 15A-2
Magnification: 600×
Voltage: 20 kV



SEM: 6
Excipient: Calcium carbonate
Manufacturer: Whittaker, Clark & Daniels
Lot No.: 15A-2
Magnification: 2400×
Voltage: 20 kV



10 Typical Properties

Acidity/alkalinity: pH = 9.0 (10% w/v aqueous dispersion)
Density (bulk): 0.8 g/cm^3
Density (tapped): 1.2 g/cm^3
Flowability: cohesive.
Hardness (Mohs): 3.0 for *Millicarb*.
Melting point: decomposes at 825°C.
Moisture content: *see* Figure 1.
Particle size: *see* Figure 2.
Refractive index: 1.59
Solubility: practically insoluble in ethanol (95%) and water. Solubility in water is increased by the presence of ammonium salts or carbon dioxide. The presence of alkali hydroxides reduces solubility.
Specific gravity: 2.7
Specific surface area: 6.21–6.47 m^2/g

11 Stability and Storage Conditions

Calcium carbonate is stable and should be stored in a well-closed container in a cool, dry place.

12 Incompatibilities

Incompatible with acids and ammonium salts (*see also* Sections 10 and 18).

13 Method of Manufacture

Calcium carbonate is prepared by double decomposition of calcium chloride and sodium bicarbonate in aqueous solution. Density and fineness are governed by the concentrations of the solutions. Calcium carbonate is also obtained from the naturally occurring minerals aragonite, calcite, and vaterite.

14 Safety

Calcium carbonate is mainly used in oral pharmaceutical formulations and is generally regarded as a nontoxic material. However, calcium carbonate administered orally may cause constipation and flatulence. Consumption of large quantities (4–60 g daily) may also result in hypercalcemia or renal impairment.[7] Therapeutically, oral doses of up to about 1.5 g are employed as an antacid. In the treatment of hyperphosphatemia in patients with chronic renal failure, oral daily doses of 2.5–17 g have been used. Calcium carbonate may interfere with the absorption of other drugs from the gastrointestinal tract if administered concominantly.

LD_{50} (rat: oral) 6.45 g/kg

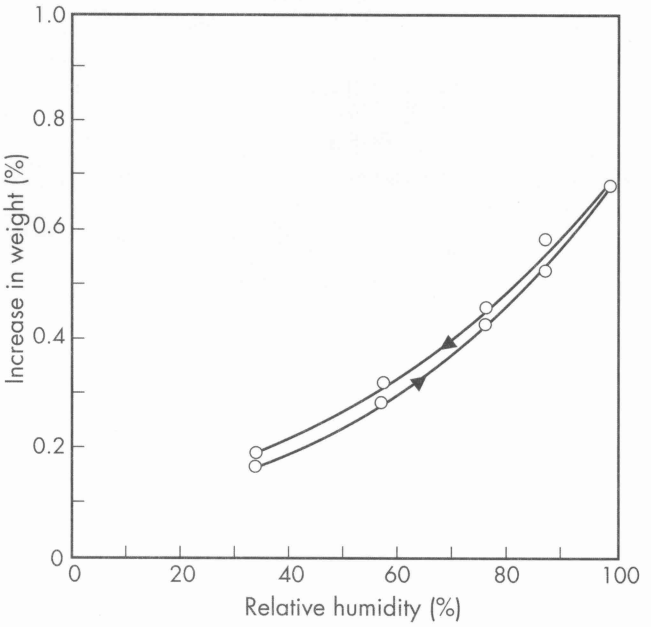


Figure 1: Moisture sorption–desorption isotherm of calcium carbonate.

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Calcium carbonate may be irritant to the eyes and on inhalation. Eye protection, gloves, and a dust mask are recommended. Calcium carbonate should be handled in a well-ventilated environment. In the UK, the long-term (8-hour TWA) occupational exposure limit for calcium carbonate is 10 mg/m^3 for total inhalable dust and 4 mg/m^3 for respirable dust.[8]

16 Regulatory Status

GRAS listed. Accepted for use as a food additive in Europe. Included in FDA Inactive Ingredients Guide (oral capsules and tablets; otic solutions). Included in nonparenteral medicines licensed in the UK.

17 Related Substances

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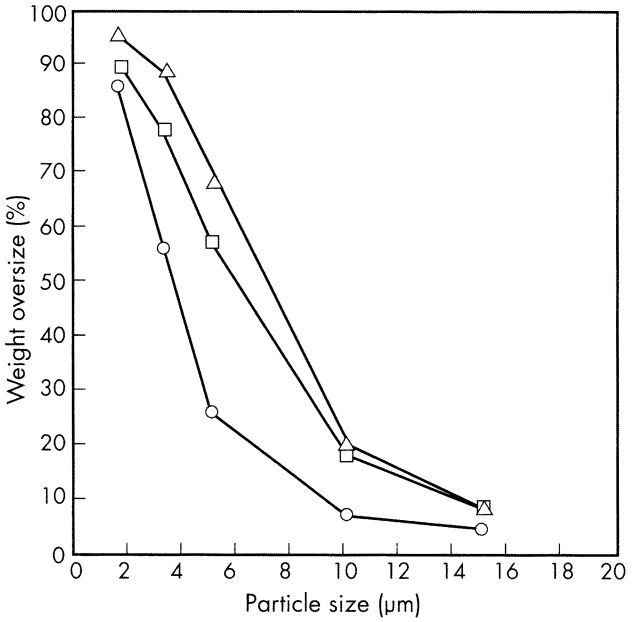

Figure 2: Particle-size distribution of calcium carbonate (*Sturcal*, Rhodia).
○: *Sturcal F*
□: *Sturcal H*
△: *Sturcal L*

18 Comments

When calcium carbonate is used in tablets containing aspirin and related substances, traces of iron may cause discoloration. This may be overcome by inclusion of a suitable chelating agent. Grades with reduced lead levels are commercially available for use in antacids and calcium supplements.

Directly compressible tablet diluents containing calcium carbonate and other excipients are commercially available. Examples of such grades are *Barcroft CS90* (containing 10% starch), *Barcroft CX50* (containing 50% sorbitol), and *Barcroft CZ50* (containing 50% sucrose) available from SPI Pharma. Available from DMV International, are *Cal-Carb 4450 PG* (containing maltodextrin), and *Cal-Carb 4457* and *Cal-Carb 4462* (both containing pregelatinized corn starch).

A directly compressible grade of calcium carbonate alone is also commercially available (*Vivapress Ca*, J. Rettenmaier and Söhne).

The EINECS number for calcium carbonate is 207-439-9.

19 Specific References

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2 Gorecki DKJ, Richardson CJ, Pavlakidis P, Wallace SM. Dissolution rates in calcium carbonate tablets: a consideration in product selection. *Can J Pharm* 1989; **122**: 484–487, 508.
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4 Haines-Nutt RF. The compression properties of magnesium and calcium carbonates. *J Pharm Pharmacol* 1976; **28**: 468–470.
5 Mattsson S, Nystrom C. Evaluation of strength-enhancing factors of a ductile binder in direct compression of sodium bicarbonate and calcium carbonate powders. *Eur J Pharm Sci* 2000; **10**(1): 53–66.
6 Kaus LC. Buffers and buffering agents. In: Swarbrick J, Boylan JC, eds. *Encyclopaedia of Pharmaceutical Technology*, vol. 2. New York: Marcel Dekker, 1988: 213–231.
7 Orwoll ES. The milk-alkali syndrome: current concepts. *Ann Intern Med* 1982; **97**: 242–248.
8 Health and Safety Executive. *EH40/2002: Occupational Exposure Limits 2002*. Sudbury: Health and Safety Executive, 2002.

20 General References

Roberts DE, Rogers CM, Richards CE, Lee MG. Calcium carbonate mixture. *Pharm J* 1986; **236**: 577.

21 Author

NA Armstrong.

22 Date of Revision

14 October 2002.