Calcium Sulfate

1 Nonproprietary Names

BP: Calcium sulphate dihydrate
PhEur: Calcii sulfas dihydricus
USPNF: Calcium sulfate

2 Synonyms

Calcium sulfate anhydrous: anhydrite; anhydrous gypsum; anhydrous sulfate of lime; *Destab*; *Drierite*; E516; karstenite; muriacite; *Snow White*.

Calcium sulfate dihydrate: alabaster; *Cal-Tab*; *Compactrol*; *Destab*; E516; gypsum; light spar; mineral white; native calcium sulfate; precipitated calcium sulfate; satinite; satin spar; selenite; terra alba; *USG Terra Alba*.

3 Chemical Name and CAS Registry Number

Calcium sulfate [7778-18-9]
Calcium sulfate dihydrate [10101-41-4]

4 Empirical Formula and Molecular Weight

Empirical Formula	Molecular Weight
$CaSO_4$	136.14
$CaSO_4 \cdot 2H_2O$	172.17

5 Structural Formula

$CaSO_4$
$CaSO_4 \cdot 2H_2O$

6 Functional Category

Tablet and capsule diluent. The anhydrous form is used as a desiccant.

7 Applications in Pharmaceutical Formulation or Technology

Calcium sulfate dihydrate is used in the formulation of tablets and capsules. In granular form it has good compaction properties and moderate disintegration properties.[1,2]

Calcium sulfate hemihydrate (*see* Section 17), is used in the preparation of plaster of Paris bandage, which is used for the immobilization of limbs and fractures; it should not be used in the formulation of tablets or capsules.

Anhydrous calcium sulfate is hygroscopic and uptake of water can cause the tablets to become very hard and to fail to disintegrate on storage. It is not recommended for the formulation of tablets, capsules, or powders for oral administration.

Therapeutically, calcium sulfate is used in dental and craniofacial surgical procedures.[3,4]

8 Description

A white or off-white, fine, odorless, and tasteless powder or granules.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for calcium sulfate.

Test	PhEur 2002	USPNF 20
Identification	+	+
Characters	+	—
Acidity or alkalinity	+	—
Arsenic	≤10 ppm	—
Chlorides	≤300 ppm	—
Heavy metals	≤20 ppm	≤0.001%
Iron	≤100 ppm	≤0.01%
Loss on drying	— —	≤1.5% 19.0–23.0%
Anhydrous		
Dihydrate		
Loss on ignition	18.0–22.0%	—
Assay	98.0–102.0%	98.0–101.0%

10 Typical properties

Acidity/alkalinity:
pH = 7.3 (10% slurry) for dihydrate
pH = 10.4 (10% slurry) for anhydrous material

Angle of repose: 37.6° for *Compactrol*.[2]

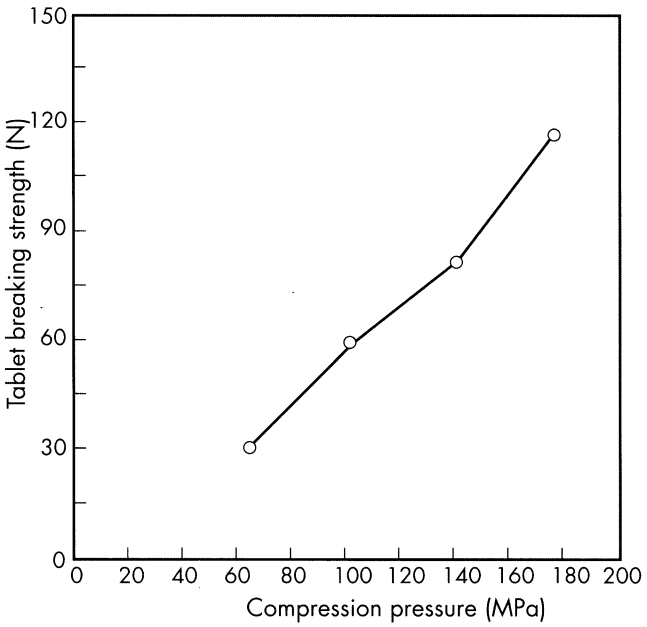

Figure 1: Compression characteristics of calcium sulfate dihydrate. Tablet weight: 700 mg.

Density (bulk):
0.94 g/cm^3 for *Compactrol* [2]
0.67 g/cm^3 for dihydrate
0.70 g/cm^3 for anhydrous material

Density (tapped):
1.10 g/cm^3 for *Compactrol* [2]
1.12 g/cm^3 for dihydrate
1.28 g/cm^3 for anhydrous material
Density (true): 2.308 g/cm^3
Flowability: 48.4% (Carr compressibility index); 5.2 g/s for *Compactrol*.[2]
Melting point: 1450°C for anhydrous material.
Particle size distribution: 93% less than 45 μm in size for the dihydrate (*USG Terra Alba*); 97% less than 45 μm in size for the anhydrous material (*Snow White*). Average particle size is 17 μm for the dihydrate and 8 μm for the anhydrous material. For *Compactrol*, not less than 98% passes through a #40 screen (425 μm), and not less than 85% is retained in a #140 screen (100 μm).
Solubility: *see* Table II.

Table II: Solubility of calcium sulfate dihydrate.

Solvent	Solubility at 20°C unless otherwise stated
Ethanol (95%)	Practically insoluble
Water	1 in 375
	1 in 485 at 100°C

Specific gravity:
2.32 for dihydrate
2.96 for anhydrous material
Specific surface area: 3.15 m^2/g (Strohlein apparatus)

11 Stability and Storage Conditions

Calcium sulfate is chemically stable. Anhydrous calcium sulfate is hygroscopic and may cake on storage. Store in a well-closed container in a dry place, avoiding heat.

12 Incompatibilities

In the presence of moisture, calcium salts may be incompatible with amines, amino acids, peptides, and proteins, which may form complexes. Calcium salts will interfere with the bioavailability of tetracycline antibiotics.[5] It is also anticipated that calcium sulfate would be incompatible with indomethacin,[6] aspirin,[7] aspartame,[8] ampicillin,[9] cephalexin,[10] and erythromycin[11] since these materials are incompatible with other calcium salts.

Calcium sulfate may react violently, at high temperatures, with phosphorus and aluminum powder; it can react violently with diazomethane.

13 Method of Manufacture

Anhydrous calcium sulfate occurs naturally as the mineral anhydrite. The naturally occurring rock gypsum may be crushed and ground for use as the dihydrate or calcined at 150°C to produce the hemihydrate. A purer variety of calcium sulfate may also be obtained chemically by reacting calcium carbonate with sulfuric acid or by precipitation from calcium chloride and a soluble sulfate.

14 Safety

Calcium sulfate dihydrate is used as an excipient in oral capsule and tablet formulations. At the levels at which it is used as an excipient, it is generally regarded as nontoxic. However, ingestion of a sufficiently large quantity can result in obstruction of the upper intestinal tract after absorption of moisture.

Owing to the limited intestinal absorption of calcium from its salts, hypercalcemia cannot be induced even after the ingestion of massive oral doses.

Calcium salts are soluble in bronchial fluid. Pure salts do not induce pneumoconiosis.

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. The fine-milled grades can generate nuisance dusts that may be irritant to the eyes or on inhalation. The use of a respirator or dust mask is recommended to prevent excessive powder inhalation since excessive inhalation may saturate the bronchial fluid, leading to precipitation and thus blockage of the air passages.

16 Regulatory Status

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

17 Related Substances

Calcium phosphate, dibasic anhydrous; calcium phosphate, dibasic dihydrate; calcium phosphate, tribasic; calcium sulfate hemihydrate.

Calcium sulfate hemihydrate

Empirical formula: $CaSO_4 \cdot \frac{1}{2}H_2O$
Molecular weight: 145.14
CAS number: [26499-65-0]
Synonyms: annalin; calcii sulfas hemihydricus; calcined gypsum; dried calcium sulfate; dried gypsum; E516; exsiccated calcium sulfate; plaster of Paris; sulfate of lime; yeso blanco.
Appearance: a white or almost white, odorless, crystalline, hygroscopic powder.
Solubility: practically insoluble in ethanol (95%); slightly soluble in water; more soluble in dilute mineral acids.
Comments: the BP 2001 defines dried calcium sulfate as predominantly the hemihydrate, produced by drying powdered gypsum ($CaSO_4 \cdot 2H_2O$) at about 150°C, in a controlled manner, such that minimum quantities of the anhydrous material are produced. Dried calcium sulfate may also contain suitable setting accelerators or decelerators.

18 Comments

Calcium sulfate will absorb moisture and therefore should be used with caution in the formulation of products containing drugs that easily decompose in the presence of moisture. The EINECS number for calcium sulfate is 231-900-3.

19 Specific References

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20 General References

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21 Author

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22 Date of Revision

17 October 2002.