

Potassium Chloride

1 Nonproprietary Names

BP: Potassium chloride
JP: Potassium chloride
PhEur: Kalii chloridum
USP: Potassium chloride

2 Synonyms

Chloride of potash; chloropotassuril; dipotassium dichloride; E508; potassium monochloride.

3 Chemical Name and CAS Registry Number

Potassium chloride [7447-40-7]

4 Empirical Formula Molecular Weight

KCl 74.55

5 Structural Formula

KCl

6 Functional Category

Therapeutic agent; tonicity agent.

7 Applications in Pharmaceutical Formulation or Technology

Potassium chloride is widely used in a variety of parenteral and nonparenteral pharmaceutical formulations. Its primary use, in parenteral and ophthalmic preparations, is to produce isotonic solutions.

Potassium chloride is also used therapeutically in the treatment of hypokalemia.

Many solid-dosage forms of potassium chloride exist including: tablets prepared by direct compression⁽¹⁻⁴⁾ and granulation;^(5,6) effervescent tablets; coated, sustained-release tablets;⁽⁷⁻¹⁰⁾ sustained-release wax matrix tablets;⁽¹¹⁾ micro-capsules;⁽¹²⁾ pellets; and osmotic pump formulations.^(13,14)

Experimentally, potassium chloride is frequently used as a model drug in the development of new solid-dosage forms, particularly for sustained-release or modified-release products.

Potassium chloride is also used widely in the food industry as a dietary supplement, pH control agent, stabilizer, thickener, and gelling agent. It can also be used in infant formulations.

8 Description

Potassium chloride occurs as odorless, colorless crystals or a white crystalline powder, with an unpleasant, saline taste. The crystal lattice is a face-centered cubic structure.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for potassium chloride.

Test	JP 2001	PhEur 2002	USP 25
Identification	+	+	+
Acidity or alkalinity	+	+	+
Appearance of solution	+	+	—
Loss on drying	≤0.5%	≤1.0%	≤1.0%
Iodide or bromide	+	+	+
Aluminum	—	≤1 ppm	≤1 ppm
Arsenic	≤2 ppm	—	—
Barium	—	+	—
Calcium and magnesium	+	≤200 ppm	+
Heavy metals	≤5 ppm	≤10 ppm	≤0.001%
Iron	—	≤20 ppm	—
Sodium	+	≤0.1%	+
Sulfates	—	≤300 ppm	—
Organic volatile impurities	—	—	+
Assay (dried basis)	≥99.0%	99.0–100.5%	99.0–100.5%

10 Typical Properties

Acidity/alkalinity: pH ≈ 7 for a saturated aqueous solution at 15°C.

Boiling point: sublimates at 1500°C

Compressibility: see Figure 1.^(3,4)

Density: 1.99 g/cm³; 1.17 g/cm³ for a saturated aqueous solution at 15°C.

Melting point: 790°C

Osmolarity: a 1.19% w/v solution is iso-osmotic with serum.

Particle size distribution: typical distribution⁽⁵⁾ is 10% less than 30 μm, 50% less than 94 μm, and 90% less than 149 μm in size. Mean particle diameter is 108 μm. Finer powders may be obtained by milling.

Solubility: see Table II.

Table II: Solubility of potassium chloride.

Solvent	Solubility at 20°C unless otherwise stated
Acetone	Practically insoluble
Ethanol (95%)	1 in 250
Ether	Practically insoluble
Glycerin	1 in 14
Water	1 in 2.8
	1 in 1.8 at 100°C

Specific surface area: 0.084 m²/g (BET method)⁽⁵⁾

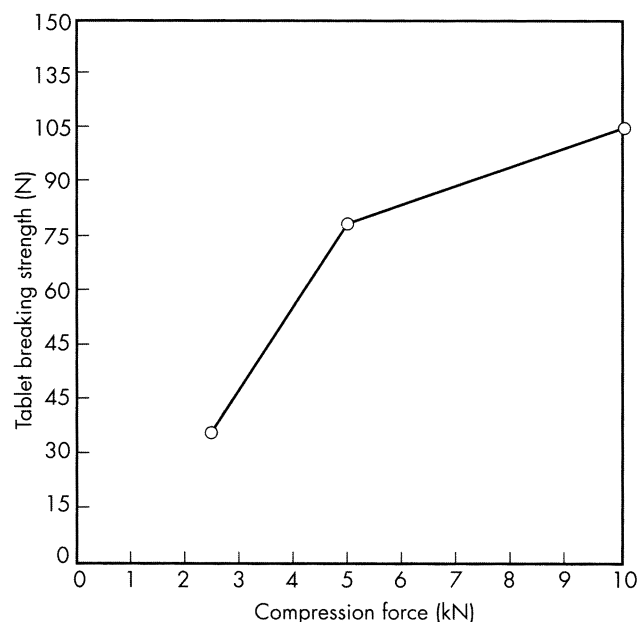


Figure 1: Compression characteristics of potassium chloride.⁽³⁾
Tablet diameter = 10 mm.

11 Stability and Storage Conditions

Potassium chloride tablets become increasingly hard on storage at low humidities. However, tablets stored at 76% relative humidity showed no increase or only a slight increase in hardness.⁽²⁾ The addition of lubricants, such as 2% w/w magnesium stearate,⁽¹⁾ reduces tablet hardness and hardness on aging.⁽²⁾ Aqueous potassium chloride solutions may be sterilized by autoclaving or by filtration.

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

12 Incompatibilities

Potassium chloride reacts violently with bromine trifluoride and with a mixture of sulfuric acid and potassium permanganate. The presence of hydrochloric acid, sodium chloride, and magnesium chloride decreases the solubility of potassium chloride in water. Aqueous solutions of potassium chloride form precipitates with lead and silver salts.

Intravenous aqueous potassium chloride solutions are incompatible with protein hydrolysate.

13 Method of Manufacture

Potassium chloride occurs naturally as the mineral sylvite or sylvine; it also occurs in other minerals such as sylvinit, carnallite, and kainite. Commercially, potassium chloride is obtained by the solar evaporation of brine or by the mining of mineral deposits.

14 Safety

Potassium chloride is used in a large number of pharmaceutical formulations including oral, parenteral, and topical preparations both as an excipient and as a therapeutic agent.

Potassium ions play an important role in cellular metabolism and imbalances can result in serious clinical effects. Orally ingested potassium chloride is rapidly absorbed from the

gastrointestinal tract and excreted by the kidneys. Potassium chloride is more irritant than sodium chloride when administered orally, and ingestion of large quantities of potassium chloride can cause effects such as gastrointestinal irritation, nausea, vomiting, and diarrhea.

High localized concentrations of potassium chloride in the gastrointestinal tract can cause ulceration, hence the development of the many enteric-coated and wax matrix sustained-release preparations that are available.⁽¹⁵⁾ Although it is claimed that some formulations cause less ulceration than others, it is often preferred to administer potassium chloride as an aqueous solution. However, solutions have also been associated with problems, mainly due to their unpleasant taste.

Parenterally, rapid injection of strong potassium chloride solutions can cause cardiac arrest; in the adult, solutions should be infused at a rate not greater than 750 mg/hour.

Therapeutically, in adults, up to 10 g orally, in divided doses has been administered daily, while intravenously up to 6 g daily has been used.

LD₅₀ (guinea pig, oral): 2.5 g/kg⁽¹⁶⁾

LD₅₀ (mouse, IP): 1.18 g/kg

LD₅₀ (mouse, IV): 0.12 g/kg

LD₅₀ (mouse, oral): 0.38 g/kg

LD₅₀ (rat, IP): 0.66 g/kg

LD₅₀ (rat, IV): 0.14 g/kg

LD₅₀ (rat, oral): 2.6 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled.

16 Regulatory Status

GRAS listed. Accepted as a food additive in Europe. Included in the FDA Inactive Ingredients Guide (injections, ophthalmic preparations, oral capsules, and tablets). Included in nonparenteral and parenteral medicines licensed in the UK.

17 Related Substances

Sodium chloride.

18 Comments

Each gram of potassium chloride represents approximately 13.4 mmol of potassium; 1.91 g of potassium chloride is approximately equivalent to 1 g of potassium.

For diets where the intake of sodium chloride is restricted, salt substitutes for use in cooking or as table salt are available and contain mainly potassium chloride, e.g., *LoSalt* (Klinge Chemicals Ltd) is a blend of 2/3 potassium chloride and 1/3 sodium chloride with magnesium carbonate added as a flow-promoting agent.

The EINECS number for potassium chloride is 231-211-8.

19 Specific References

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20 General References

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22 Date of Revision

7 May 2002.