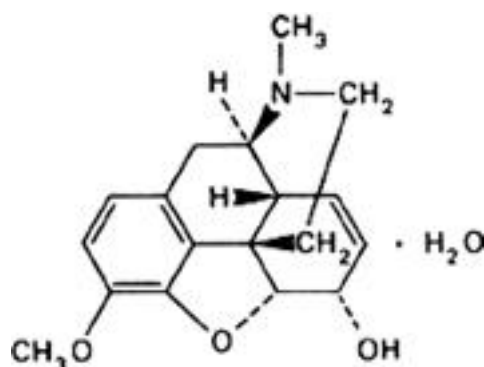


Codeine monohydrate (Codeinum monohydricum)**Molecular formula.** $C_{18}H_{21}NO_3 \cdot H_2O$ **Relative molecular mass.** 317.4**Graphic formula.****Chemical name.** 7,8-Didehydro-4,5 α -epoxy-3-methoxy-17-methylmorphinan-6 α -ol monohydrate; CAS Reg. No. 6059-47-8.**Description.** Colourless crystals or a white, crystalline powder; odourless.**Solubility.** Slightly soluble in water; freely soluble in ethanol (~750 g/l) TS and ether R.**Category.** Antitussive; analgesic.**Storage.** Codeine monohydrate should be kept in a tightly closed container, protected from light.**Additional information.** Codeine monohydrate effloresces slowly in dry air.**Requirements****Definition.** Codeine monohydrate contains not less than 99.0% and not more than 101.0% of $C_{18}H_{21}NO_3$, calculated with reference to the dried substance.**Identity tests**

- A. Dissolve 5 mg in 1 mL of sulfuric acid (~1760 g/l) TS, add 1 drop of ferric chloride (25 g/l) TS, and warm on a water-bath; a blue colour is produced, which changes to red on the addition of 1 drop of nitric acid (~130 g/l) TS.
- B. Dissolve 1 mg in 0.5 mL of selenious acid/sulfuric acid TS; a green colour is produced, which rapidly changes to blue, then slowly to dark yellow-green.
- C. Melting temperature, about 156°C.

Specific optical rotation. Use a 20 mg/mL solution in ethanol (~750 g/l) TS and calculate with reference to the dried substance;

$$[\alpha]_D^{20} = -142^\circ \text{ to } -146^\circ.$$

Clarity and colour of solution. A solution of 0.050 g in 10 mL of water is clear and colourless.**Sulfated ash.** Not more than 1.0 mg/g.**Loss on drying.** Dry to constant weight at 105°C; it loses not less than 50 mg/g and not more than 60 mg/g.**pH value.** pH of a 5.0 mg/mL solution in carbon-dioxide-free water R, not less than 9.0.**Related alkaloids.** Carry out the test as described under [1.14.1 Chromatography, Thin-layer chromatography](#), using silica gel R1 as the coating substance and a mixture of 72 volumes of ethanol (~750 g/l) TS, 30 volumes of cyclohexane R, and 6 volumes of ammonia (~260 g/l) TS as the mobile phase. Apply separately to the plate 10 μ l of each of 2 solutions in a mixture of 4 volumes of hydrochloric acid (0.01 mol/l) VS and 1 volume of ethanol (~750 g/l) TS containing (A) 50 mg of the test substance per mL and (B) 0.66 mg of the test substance per mL. After removing the plate from the chromatographic chamber, allow it to dry in air, spray with potassium iodobismuthate TS2, and examine the chromatogram in daylight. Any spot obtained with solution A, other than the principal spot, is not more intense than that obtained with solution B.**Assay.** Dissolve about 0.25 g, accurately weighed, in 30 mL of glacial acetic acid R1, add 10 mL of acetic anhydride R, and titrate with perchloric acid (0.1 mol/l) VS as described under [2.6 Non-aqueous titration](#), Method A. Each mL of perchloric acid (0.1 mol/l) VS is equivalent to 29.94 mg of $C_{18}H_{21}NO_3$.