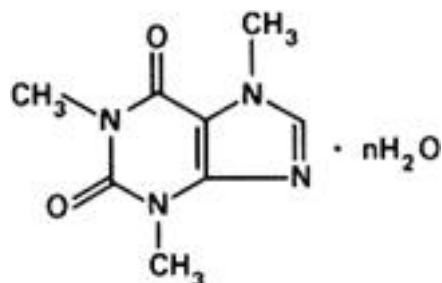


Caffeine (Coffeinum)**Caffeine anhydrous****Caffeine monohydrate**

Molecular formula. $C_8H_{10}N_4O_2$ (anhydrous); $C_8H_{10}N_4O_2 \cdot H_2O$ (monohydrate).

Relative molecular mass. 194.2 (anhydrous); 212.2 (monohydrate).

Graphic formula.



n = 0 (anhydrous)

n = 1 (monohydrate)

Chemical name. 3,7-Dihydro-1,3,7-trimethyl-1*H*-purine-2,6-dione; CAS Reg. No. 58-08-2 (anhydrous). 3,7-Dihydro-1,3,7-trimethyl-1*H*-purine-2,6-dione monohydrate; CAS Reg. No. 5743-12-4 (monohydrate).

Description. Silky, colourless crystals or a white, crystalline powder; odourless.

Solubility. Soluble in 60 parts of water and in 100 parts of ethanol (~750 g/l) TS; slightly soluble in ether R.

Category. Central nervous stimulant.

Storage. Caffeine should be kept in a well-closed container.

Labelling. The designation on the container of Caffeine should state whether the substance is the monohydrate or is in the anhydrous form.

Additional information. Caffeine monohydrate is efflorescent in air.

Requirements

Definition. Caffeine contains not less than 98.5% and not more than 101.0% of $C_8H_{10}N_4O_2$, calculated with reference to the dried substance.

Identity tests

• Either test A alone or all 3 tests B, C, and D may be applied.

A. Carry out the examination as described under [1.7 Spectrophotometry in the infrared region](#). For Caffeine monohydrate, the substance must be previously dried to constant weight at 80°C. The infrared absorption spectrum is concordant with the spectrum obtained from caffeine RS or with the *reference spectrum* of caffeine.

B. To 10 mg, contained in a porcelain dish, add 1 mL of hydrochloric acid (~250 g/l) TS and 0.5 mL of hydrogen peroxide (~60 g/l) TS, and evaporate to dryness on a water-bath. Add 1 drop of ammonia (~100 g/l) TS; the residue acquires a purple colour, which disappears upon the addition of 2-3 drops of sodium hydroxide (~80 g/l) TS.

C. To a saturated solution add a few drops of iodine TS; the solution remains clear. Add a few drops of hydrochloric acid (~70 g/l) TS; a brown precipitate is produced. On neutralization with sodium hydroxide (~80 g/l) TS, the precipitate dissolves.

D. Melting temperature, after drying at 80°C, about 236°C.

Clarity and colour of solution. A solution of 5.0 g in 10 mL of boiling water is clear and colourless.

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry to constant weight at 80°C: Caffeine (anhydrous) loses not more than 5.0 mg/g. Caffeine monohydrate loses not less than 50 mg/g and not more than 90 mg/g.

pH value. pH of a 10 mg/mL solution in carbon-dioxide-free water R, 4.8-6.6.

Related substances. Carry out the test as described under [1.14.1 Chromatography, Thin-layer chromatography](#), using silica gel R2 as the coating substance and a mixture of 4 volumes of 1-butanol R, 3 volumes of chloroform R, and 1 volume of ammonia (~260 g/l) TS as the mobile phase. Prepare 2 solutions in a mixture of 6 volumes of chloroform R and 4 volumes of methanol R containing (A) 20 mg of the test substance per mL and (B) 0.20 mg of the test substance per mL. Apply separately to the plate 10 μ l of solution A and 5 μ l of solution B. After removing the plate from the chromatographic chamber, allow it to dry in air, and examine the chromatogram in ultraviolet light (254 nm). Any spot obtained with solution A, other than the principal spot, is not more intense than that obtained with solution B.

Assay. Dissolve about 0.18 g, accurately weighed, in 10 mL of acetic anhydride R and 20 mL of toluene 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 19.42 mg of $C_8H_{10}N_4O_2$.