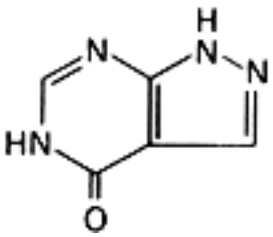
Allopurinol (Allopurinolum)

Molecular formula. $C_5H_4N_4O$

Relative molecular mass. 136.1

Graphic formula.



Chemical name. 1,5-Dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one; 1-*H*-pyrazolo[3,4-*d*]pyrimidin-4-ol; CAS Reg. No. 315-30-0.

Description. A white or almost white, microcrystalline powder; odourless or almost odourless.

Solubility. Very slightly soluble in water and in ethanol (~750 g/l) TS and ether R.

Category. Xanthine oxidase inhibitor.

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

Requirements

Definition. Allopurinol contains not less than 98.0% and not more than 101.0% of $C_5H_4N_4O$, calculated with reference to the dried substance.

Identity tests

A. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from allopurinol RS or with the *reference spectrum* of allopurinol.

B. Dissolve 0.1 g in 10 mL of sodium hydroxide (0.1 mol/l) VS and add sufficient hydrochloric acid (0.1 mol/l) VS to produce 100 mL; dilute 10 mL to 100 mL with hydrochloric acid (0.1 mol/l) VS and dilute 10 mL of this solution again to 100 mL with hydrochloric acid (0.1 mol/l) VS. The absorption spectrum of the resulting solution, when observed between 230 nm and 350 nm, exhibits a maximum at about 250 nm and a minimum at about 231 nm. The absorbance at the maximum wavelength is about 0.55. The ratio of the absorbance of a 1-cm layer at 231 nm to that at 250 nm is between 0.52 and 0.62.

C. Dissolve 0.05 g in 5 mL of sodium hydroxide (~80 g/l) TS, add 1 mL of alkaline potassio-mercuric iodide TS, heat to boiling, and allow to stand; a yellow, flocculent precipitate is produced.

Heavy metals. Use 1.0 g for the preparation of the test solution as described under 2.2.3 Limit test for heavy metals, Procedure 3; determine the heavy metals content according to Method A; not more than 20 µg/g.

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry to constant weight at 105°C; it loses not more than 5.0 mg/g.

Related substances. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using cellulose R3 as the coating substance. Prepare the mobile phase by shaking 200 mL of 1-butanol R with 200 mL of ammonia (~100 g/l) TS. Apply separately to the plate 10 µl of each of 2 freshly prepared solutions in diethylamine R containing (A) 25 mg of the test substance per mL and (B) 0.050 mg of 3-aminopyrazole-4-carboxamide hemisulfate RS per mL. 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 0.25 g, accurately weighed, in 50 mL of dimethylformamide R, add 2 drops of thymol blue/dimethylformamide TS and titrate with sodium methoxide (0.1 mol/l) VS to a blue end-point, as described under 2.6 Non-aqueous titration, Method B. Each mL of sodium methoxide (0.1 mol/l) VS is equivalent to 13.61 mg of $C_5H_4N_4O$.