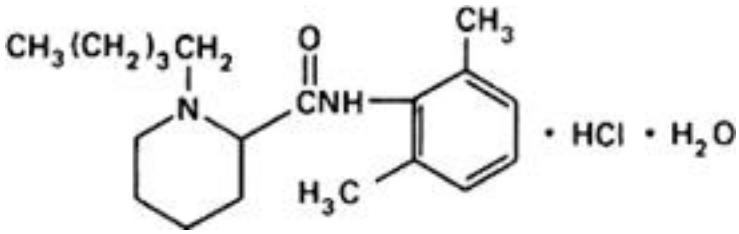
Bupivacaine hydrochloride (Bupivacaini hydrochloridum)

Molecular formula. $C_{18}H_{28}N_2O,HCl,H_2O$

Relative molecular mass. 342.9

Graphic formula.



Chemical name. 1-Butyl-2',6'-pipecoloxylidide monohydrochloride monohydrate; 1-butyl-*N*-(2,6-dimethylphenyl)-2-piperidinecarboxamide monohydrochloride monohydrate; CAS Reg. No. 73360-54-0.

Description. A white, crystalline powder; odourless.

Solubility. Soluble in 25 parts of water and in 8 parts of ethanol (~750 g/l) TS; slightly soluble in ether R.

Category. Local anaesthetic.

Storage. Bupivacaine hydrochloride should be kept in a well-closed container.

Requirements

Definition. Bupivacaine hydrochloride contains not less than 98.5% and not more than 101.0% of $C_{18}H_{28}N_2O,HCl$, 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 bupivacaine hydrochloride RS or with the *reference spectrum* of bupivacaine hydrochloride.

B. Dissolve 0.15 g in 10 mL of water and add 20 mL of trinitrophenol (7 g/l) TS. Heat the mixture to boiling, allow to cool and, if necessary, scrape the inner surface of the beaker to induce crystallization; wash the precipitate rapidly with a small quantity of water, followed by successive quantities of methanol R and ether R, using 2 mL each time; melting temperature about 194°C (bupivacaine picrate).

C. A 2 mg/mL solution yields reaction B, described under 2.1 General identification tests as characteristic of chlorides.

Copper. To 0.25 g in 10 mL of water, add 0.25 mL of disodium edetate (0.05 mol/l) VS, and allow to stand for 2 minutes; add 0.2 g of copper-free citric acid R, 1 mL of ammonia (~100 g/l) TS and 1 mL of sodium diethyldithiocarbamate (0.8 g/l) TS and extract with 10 mL of carbon tetrachloride R for 2 minutes. The colour of the extract is not deeper than that of the extract obtained when 10 mL of a mixture of 3 volumes of copper (II) sulfate (80 g/l) TS and 397 volumes of water are similarly treated.

Iron. Ignite 1.0 g with 1 g of anhydrous sodium carbonate FeR; cool and dissolve the residue in 5 mL of hydrochloric acid (~250 g/l) FeTS and 30 mL of water. Treat the solution as described under 2.2.4 Limit test for iron, using 0.5 mL of iron standard FeTS; the iron content is not more than 10 µg/g.

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry to constant weight at 105°C; it loses not less than 45 mg/g and not more than 60 mg/g.

pH value. pH of a 10 mg/mL solution, 4.5-6.0.

Absorption in the ultraviolet region. The absorption spectrum of a 0.4 mg/mL solution in hydrochloric acid (0.01 mol/l) VS, when observed between 230 nm and 350 nm, exhibits 2 maxima at about 263 nm and 271 nm. The absorbance of a 1-cm layer at the maximum wavelength of 263 nm is not less than 0.53 and not more than 0.58, and at the maximum wavelength of 271 nm is not less than 0.43 and not more than 0.48 (preferably use 2-cm cells for the measurements and calculate the absorbances of 1-cm layers).

Related substances. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R1 as the coating substance and ethanol (~750 g/l) TS as the mobile phase. Apply separately to the plate 2 µl of each of 2 solutions in methanol R containing (A) 50 mg of the test substance per mL and (B) 0.50 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 0.65 g, accurately weighed, in 30 mL of glacial acetic acid R1, add 10 mL of mercuric/acetic acid TS, 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 32.49 mg of $C_{18}H_{28}N_2O$,HCl.

Additional requirements for Bupivacaine hydrochloride for parenteral use

Complies with the monograph for "Parenteral preparations".

Bacterial endotoxins. Carry out the test as described under 3.4 Test for bacterial endotoxins; contains not more than 2.5 IU of endotoxin RS per mg.