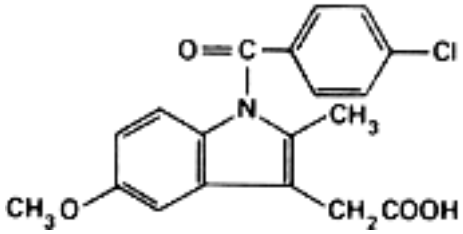
Indometacin (Indometacinum)

Molecular formula. $C_{19}H_{16}ClNO_4$

Relative molecular mass. 357.8

Graphic formula.



Chemical name. 1-(*p*-Chlorobenzoyl)-5-methoxy-2-methylindole-3-acetic acid; 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indole-3-acetic acid; CAS Reg. No. 53-86-1.

Description. A white or a pale yellow, crystalline powder; odourless or almost odourless.

Solubility. Practically insoluble in water; sparingly soluble in ethanol (~750 g/l) TS and ether R.

Category. Analgesic; anti-inflammatory.

Storage. Indometacin should be kept in a well-closed container, protected from light.

Additional information. Indometacin exhibits polymorphism. The polymorph specified in the monograph corresponds to the crystal form of indometacin RS.

Requirements

Definition. Indometacin contains not less than 98.0% and not more than 101.0% of $C_{19}H_{16}ClNO_4$, calculated with reference to the dried substance.

Identity tests

• Either test A alone or tests B and C may be applied.

A. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum obtained from the solid state of the test substance is concordant with the spectrum obtained from indometacin RS or with the *reference spectrum* of indometacin (confirmation of polymorphic form).

B. Dissolve 0.1 g in 100 mL of water containing 0.5 mL of sodium hydroxide (1 mol/l) VS. To a 1 mL-portion add 1 mL of freshly prepared sodium nitrite (1 g/l) TS and allow to stand for 5 minutes. Add 0.5 mL of sulfuric acid (~1760 g/l) TS; a deep yellow colour is produced. To another 1-mL portion add 1 mL of sodium nitrite (1 g/l) TS, and allow to stand for 5 minutes. Add 0.5 mL of hydrochloric acid (~420 g/l) TS; a green colour is produced.

C. Melting temperature, about 160°C.

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 2.0 mg/g.

Loss on drying. Dry to constant weight at 105°C under reduced pressure (not exceeding 0.6 kPa or about 5 mm of mercury); it loses not more than 5.0 mg/g.

Related substances. Carry out the test as described under 1.14.1 Thin-layer chromatography, using silica gel R2 as the coating substance and preparing the slurry in sodium dihydrogen phosphate (45 g/l) TS. As the mobile phase, use a mixture of 7 volumes of ether R and 3 volumes of light petroleum R. Apply separately to the plate 10 µl of each of 2 solutions in methanol R containing (A) 20 mg of the test substance per mL and (B) 0.10 mg of the test substance 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 0.33 g, accurately weighed, in 75 mL of acetone R through which nitrogen R free from carbon dioxide has previously been passed for 15 minutes. Maintain a constant stream of nitrogen through the solution and titrate with carbonate-free sodium hydroxide (0.1 mol/l) VS using phenolphthalein/ethanol TS as indicator or determining the end-point potentiometrically. Repeat the operation without the substance being examined and make any necessary corrections. Each mL of carbonate-free sodium hydroxide (0.1 mol/l) VS is equivalent to 35.78 mg of $C_{19}H_{16}ClNO_4$.