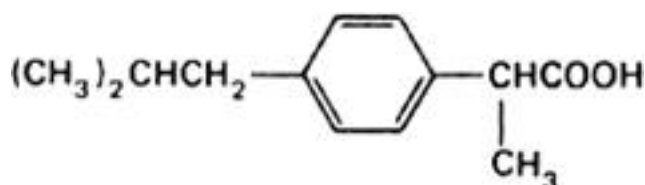


Ibuprofen (Ibuprofenum)**Molecular formula.** $C_{13}H_{18}O_2$ **Relative molecular mass.** 206.3**Graphic formula.****Chemical name.** *p*-Isobutylhydratropic acid; α -methyl-4-(2-methylpropyl)benzeneacetic acid; 2-(*p*-isobutylphenyl)propionic acid; CAS Reg. No. 15687-27-1.**Description.** Colourless crystals or a white, crystalline powder; odour, characteristic.**Solubility.** Practically insoluble in water; soluble in 1.5 parts of ethanol (~750 g/l) TS, in 2 parts of ether R and in 1.5 parts of acetone R.**Category.** Analgesic; anti-inflammatory.**Storage.** Ibuprofen should be kept in a well-closed container.**Requirements****Definition.** Ibuprofen contains not less than 98.5% and not more than 100.5% of $C_{13}H_{18}O_2$, 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 is concordant with the spectrum obtained from ibuprofen RS or with the *reference spectrum* of ibuprofen.

B. The absorption spectrum of a 0.25 mg/mL solution in sodium hydroxide (0.1 mol/l) VS, when observed between 220 nm and 350 nm, is qualitatively similar to that of a 0.25 mg/mL solution of ibuprofen RS in sodium hydroxide (0.1 mol/l) VS (maxima occur at about 264 nm and 273 nm, and a shoulder at about 259 nm). The absorbances of the solutions at the respective maxima do not differ from each other by more than 3%. The absorbance of a 1-cm layer at the wavelengths of the main maxima at 264 nm and 273 nm are about 0.46 and 0.39, respectively (preferably use 2-cm cells for the measurement and calculate the absorbances of 1-cm layers).

C. Melting temperature, about 76°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 10 μ g/g.**Sulfated ash.** Not more than 1.0 mg/g.**Loss on drying.** Dry to constant weight at ambient temperature under reduced pressure (not exceeding 0.6 kPa or about 5 mm of mercury) over phosphorus pentoxide R; it loses not more than 5.0 mg/g.**Related substances**

A. Carry out the test as described under [1.14.1 Chromatography, Gas chromatography](#), using a solution of the test substance prepared as follows: To 0.10 g add diazomethane TS until effervescence ceases and a persistent yellow colour is produced. Remove the solvent in a current of nitrogen, warming gently if necessary, and dissolve the residue in 2 mL of chloroform R. Use this solution in procedures A1 and A2.

In procedure A1 use a glass column 1.8 m long and 3.0 mm in internal diameter packed with an adsorbent composed of 1 g of macrogol 20M R and 9 g of acid-washed, silanized kieselguhr R3, and maintained at 135°C. Use nitrogen R as the carrier gas and a flame ionization detector. In this system, determine only those impurities with a relative retention time of less than 2.5, taking the retention time of ibuprofen as 1.0. The ratio of the total area of the peaks due to these impurities to the area under the peak of ibuprofen does not exceed 0.010, and the corresponding ratio for the peak of any individual impurity does not exceed 0.003.

In procedure A2 use a glass column 1.8 m long and 3.0 mm in internal diameter packed with an adsorbent composed of 0.5 g of methyl silicone gum R, 0.2 g of cyanoethylmethyl silicone gum R and 9.3 g of acid-washed, silanized kieselguhr R4 and maintained at 170°C. Use nitrogen R as the carrier gas and a flame ionization detector. In this system, determine only those impurities with a relative retention time of between 1.5 and 6.0, taking the retention time of ibuprofen as 1.0. The ratio of the total area of the peaks due to these impurities to the area under the peak of ibuprofen does not exceed 0.010.

The sum of the ratios found in procedures A1 and A2 does not exceed 0.015.

B. 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 15 volumes of 1-hexane R, 5 volumes of ethyl acetate R and 1 volume of glacial acetic acid R as the mobile phase. Apply separately to the plate 5 µl of each of 2 solutions in chloroform R containing (A) 100 mg of the test substance per mL and (B) 1 mg of the test substance per mL. After removing the plate from the chromatographic chamber, allow it to dry in air, spray very lightly with a 10 mg/mL solution of potassium permanganate R in sulfuric acid (~100 g/l) TS, heat at 120°C for 20 minutes, and examine the chromatogram in ultraviolet light (365 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 0.4 g, accurately weighed, in 100 mL of ethanol (~750 g/l) TS previously neutralized to phenolphthalein/ethanol TS, and titrate with carbonate-free sodium hydroxide (0.1 mol/l) VS, using phenolphthalein/ethanol TS as indicator. 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 20.63 mg of C₁₃H₁₈O₂.