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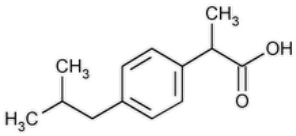
Ibuprofen



$C_{13}H_{18}O_2$ 206.28

Benzeneacetic acid, α-methyl-4-(2-methylpropyl), (±)-.

(±)-*p*-Isobutylhydratropic acid.

(±)-2-(*p*-Isobutylphenyl)propionic acid CAS RN®: 15687-27-1; UNII: WK2XYI10QM.

(±) Mixture CAS RN®: 58560-75-1.

» Ibuprofen contains not less than 97.0 percent and not more than 103.0 percent of $C_{13}H_{18}O_2$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—

USP Ibuprofen RS

USP Ibuprofen Related Compound C RS

Identification—

Change to read:

A: ▲*Spectroscopic Identification Tests* ⟨197⟩*, Infrared Spectroscopy: 197M*▲ (CN 1-May-2020) —Do not dry specimens.

Change to read:

B: ▲*Spectroscopic Identification Tests* ⟨197⟩*, Ultraviolet-Visible Spectroscopy: 197U*▲ (CN 1-May-2020)

Solution: 250 µg per mL.

Medium: 0.1 N sodium hydroxide.

Respective absorptivities at 264 nm and 273 nm, calculated on the anhydrous basis, do not differ by more than 3.0%.

C: The chromatogram of the *Assay preparation* obtained as directed in the *Assay* exhibits a major peak for ibuprofen, the retention time of which, relative to that of the internal standard, corresponds to that exhibited in the chromatogram of the *Standard preparation,* obtained as directed in the *Assay*.

Water Determination, *Method I* ⟨921⟩: not more than 1.0%.

Residue on ignition ⟨281⟩: not more than 0.5%.

Chromatographic purity—

Mobile phase—Prepare a suitable filtered mixture of water, previously adjusted with phosphoric acid to a pH of 2.5 and acetonitrile (1340:680). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Test preparation—Prepare a solution of Ibuprofen in acetonitrile containing about 5 mg per mL.

Resolution solution—Prepare a solution in acetonitrile containing in each mL about 5 mg of Ibuprofen and 5 mg of valerophenone.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 214-nm detector and a 4-mm × 15-cm column that contains 5-µm packing L1 and is maintained at 30 ± 0.5°. The flow rate is about 2 mL per minute. Chromatograph a series of 5-µL injections of the *Test preparation* to condition the column. Chromatograph the *Resolution solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.8 for valerophenone and 1.0 for ibuprofen, and the resolution, *R,* between the valerophenone peak and the ibuprofen peak is not less than 2.0.

Procedure—[Note—Use peak areas where peak responses are indicated.] Inject about 5 µL of the *Test preparation* into the chromatograph, record the chromatogram, and measure the peak responses. Calculate the percentage of each impurity taken by the formula:

$$100 r_i / r_t$$

in which r_i is the response of an individual peak, other than the solvent peak and the main ibuprofen peak, and r_t is the sum of the responses of all the peaks, excluding that of the solvent peak: not more than 0.3% of any individual impurity is found, and the sum of all the individual impurities found does not exceed 1.0%.

Limit of ibuprofen related compound C—Using the chromatograms of the *Assay preparation* and the *Ibuprofen related compound C standard solution,* obtained as directed in the *Assay,* calculate the percentage of ibuprofen related compound C ($C_{12}H_{16}O$) in the portion of Ibuprofen

taken by the formula:

$$10{,}000(C/W)(R_U/R_S)$$

in which *C* is the concentration, in mg per mL, of USP Ibuprofen Related Compound C RS in the *Ibuprofen related compound C standard solution; W* is the weight, in mg, of Ibuprofen taken to prepare the *Assay preparation;* and R_U and R_S are the peak response ratios of ibuprofen related compound C to valerophenone obtained from the *Assay preparation* and the *Ibuprofen related compound C standard solution,* respectively: not more than 0.1% is found.

Assay—

Mobile phase—Dissolve 4.0 g of chloroacetic acid in 400 mL of water, and adjust with ammonium hydroxide to a pH of 3.0. Add 600 mL of acetonitrile, filter, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Internal standard solution—Prepare a solution of valerophenone in *Mobile phase* having a concentration of about 0.35 mg per mL.

Standard preparation—Dissolve an accurately weighed quantity of USP Ibuprofen RS in *Internal standard solution* to obtain a solution having a known concentration of about 12 mg per mL.

Ibuprofen related compound C standard solution—Quantitatively dissolve an accurately weighed quantity of USP Ibuprofen Related Compound C RS in acetonitrile to obtain a solution having a known concentration of about 0.6 mg per mL. Add 2.0 mL of this stock solution to 100.0 mL of *Internal standard solution,* and mix to obtain a solution having a known concentration of about 0.012 mg of ibuprofen related compound C per mL.

Assay preparation—Transfer about 1200 mg of Ibuprofen, accurately weighed, to a 100-mL volumetric flask, dilute with *Internal standard solution* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative retention times are about 1.4 for the internal standard and 1.0 for ibuprofen; the resolution, *R,* between ibuprofen and the internal standard is not less than 2.5; and the relative standard deviation for replicate injections is not more than 2.0%. Chromatograph the *Ibuprofen related compound C standard solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 1.0 for valerophenone and 1.2 for ibuprofen related compound C; the resolution, *R,* between valerophenone and ibuprofen related compound C is not less than 2.5; the tailing factors for the individual peaks are not more than 2.5; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 5 µL) of the *Standard preparation,* the *Assay preparation,* and the *Ibuprofen related compound C standard solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{13}H_{18}O_2$ in the portion of Ibuprofen taken by the formula:

$$100C(R_U/R_S)$$

in which *C* is the concentration, in mg per mL, of USP Ibuprofen RS in the *Standard preparation;* and R_U and R_S are the peak response ratios obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
IBUPROFEN	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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