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Ibuprofen Oral Suspension

DEFINITION
Ibuprofen Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of ibuprofen ($C_{13}H_{18}O_2$).

IDENTIFICATION
• **A.** The UV absorption spectra of the ibuprofen peak of the *Sample solution* exhibit maxima and minima at the same wavelengths as those of the *Standard solution*, as obtained in the *Assay*.
• **B.** The retention time of the ibuprofen peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
• **Procedure**

Mobile phase: Dissolve 1.52 g of monobasic potassium phosphate in 560 mL of water. Adjust with phosphoric acid to a pH of 2.05 if necessary. Add 440 mL of tetrahydrofuran and mix.

Diluent: Methanol and water (1:1)

Standard solution: 0.4 mg/mL of USP Ibuprofen RS in *Diluent*

Sample solution: Nominally 0.4 mg/mL of ibuprofen in *Diluent* prepared as follows. Transfer a suitable amount of Oral Suspension to a suitable volumetric flask. Add about 60% of the final volume of *Diluent*. Sonicate for 45 min. Cool and dilute with *Diluent* to volume.

Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm. For *Identification A*, use a diode-array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L7

Flow rate: 1.0 mL/min

Injection volume: 25 µL

Run time: NLT 1.9 times the retention time of ibuprofen

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 3.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ibuprofen ($C_{13}H_{18}O_2$) in the portion of Oral Suspension taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of ibuprofen from the *Sample solution*

r_S = peak response of ibuprofen from the *Standard solution*

C_S = concentration of USP Ibuprofen RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of ibuprofen in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution ⟨711⟩**

Medium: pH 7.2 phosphate buffer (see *Reagents, Indicators, and Solutions—Buffer Solutions*); 900 mL

Apparatus 2: 50 rpm

Time: 60 min

Buffer: Dilute 0.7 mL of phosphoric acid with water to obtain 1000 mL of 0.01 M phosphoric acid.

Mobile phase: Acetonitrile and *Buffer* (37:63)

Internal standard solution: 0.3 mg/mL of benzophenone in acetonitrile

Standard stock solution: Dissolve a quantity of USP Ibuprofen RS in *Medium* to obtain a solution with a known concentration of 0.011*J* mg/mL, *J* being the labeled amount of ibuprofen in the Oral Suspension, in mg/mL.

Standard solution: *Internal standard solution* and *Standard stock solution* (1:1), passed through a suitable filter of 0.5-µm or finer pore size

Sample stock solution: Filter a portion of the solution under test.

Sample solution: *Internal standard solution* and *Sample stock solution* (1:1), passed through a suitable filter of 0.5-µm or finer pore size

Density: Using a tared 50-mL volumetric flask, weigh 50 mL of Oral Suspension that has been previously well shaken to ensure homogeneity. Allow to stand until the entrapped air has risen, and invert carefully just prior to transferring it to the volumetric flask. From the observed weight of 50 mL of Oral Suspension, calculate the density of Oral Suspension in g/mL.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for benzophenone and ibuprofen are 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between benzophenone and ibuprofen

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Using an accurately tared syringe, draw about 10 mL of well-mixed Oral Suspension into the syringe, which is connected to tubing, and weigh. [Note—The tubing of the syringe is placed into a zone that is between the surface of the *Medium* and the top of the rotating blade.] Express the Oral Suspension into the *Medium.* Promptly reweigh the syringe and determine the weight, in g, of Oral Suspension added to the *Medium.*

Calculate the percentage of the labeled amount of ibuprofen ($C_{13}H_{18}O_2$) dissolved:

$$\text{Result} = (R_U/R_S) \times C_S \times V \times (\text{▲}d\text{▲}_{\text{(ERR 1-Jun-2022)}}/W_U) \times \text{▲}D\text{▲}_{\text{(ERR 1-Jun-2022)}} \times (1/L) \times 100$$

R_U	= peak area ratio of ibuprofen to benzophenone from the *Sample solution*
R_S	= peak area ratio of ibuprofen to benzophenone from the *Standard solution*
C_S	= concentration of USP Ibuprofen RS in the *Standard solution* (mg/mL)
V	= volume of *Medium*, 900 mL
$\text{▲}d\text{▲}_{\text{(ERR 1-Jun-2022)}}$	= density of Oral Suspension (g/mL)
W_U	= weight of the portion of Oral Suspension added to the *Medium* (g)
$\text{▲}D$	= dilution factor of the *Sample solution*, 2▲ (ERR 1-Jun-2022)
L	= label claim (mg/mL)

Tolerances: NLT 80% (*Q*) of the labeled amount of ibuprofen ($C_{13}H_{18}O_2$) is dissolved.

- **Uniformity of Dosage Units ⟨905⟩**

For single-unit containers

Acceptance criteria: Meets the requirements

- **Deliverable Volume ⟨698⟩**

For multiple-unit containers

Acceptance criteria: Meets the requirements

IMPURITIES

- **Organic Impurities**

Mobile phase, Diluent, and **Sample solution:** Proceed as directed in the *Assay*.

System suitability solution: 0.4 mg/mL of USP Ibuprofen RS, 0.004 mg/mL each of USP Ibuprofen Related Compound C RS and USP Ibuprofen Related Compound J RS, and 0.0169 mg/mL of USP Benzoic Acid RS in *Diluent*

Sensitivity solution: 0.0002 mg/mL each of USP Ibuprofen Related Compound J RS and USP Ibuprofen Related Compound C RS in *Diluent*

Standard solution A: 0.0002 mg/mL of USP Ibuprofen RS in *Diluent*

Standard solution B: 0.004 mg/mL each of USP Ibuprofen Related Compound J RS and USP Ibuprofen Related Compound C RS in *Diluent*

Chromatographic system: Proceed as directed in the *Assay*, except for the *Detector*.

Detectors

For the quantitation of unspecified degradation products: UV 220 nm

For the quantitation of ibuprofen related compound C and ibuprofen related compound J: UV 254 nm

System suitability

Samples: *System suitability solution*, *Sensitivity solution*, *Standard solution A*, and *Standard solution B*

Suitability requirements

For the quantitation of unspecified degradation products

Resolution: NLT 2.0 between benzoic acid and ibuprofen related compound J; NLT 2.0 between ibuprofen related compound J and ibuprofen related compound C; NLT 2.0 between ibuprofen related compound C and ibuprofen, *System suitability solution*

Relative standard deviation: NMT 10.0%, *Standard solution A*

For the quantitation of ibuprofen related compound J and ibuprofen related compound C

Resolution: NLT 2.0 between benzoic acid and ibuprofen related compound J; NLT 2.0 between ibuprofen related compound J and ibuprofen related compound C; NLT 2.0 between ibuprofen related compound C and ibuprofen, *System suitability solution*

Relative standard deviation: NMT 2.0% for ibuprofen related compound J and ibuprofen related compound C, *Standard solution B*

Signal-to-noise ratio: NLT 10 for ibuprofen related compound J and ibuprofen related compound C, *Sensitivity solution*

Analysis

Samples: *Sample solution*, *Standard solution A*, and *Standard solution B*

Calculate the percentage of ibuprofen related compound J and ibuprofen related compound C in the portion of Oral Suspension taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of ibuprofen related compound J or ibuprofen related compound C from the *Sample solution*

r_S = peak response of ibuprofen related compound J or ibuprofen related compound C from *Standard solution B*

C_S = concentration of USP Ibuprofen Related Compound J RS or USP Ibuprofen Related Compound C RS in *Standard solution B* (mg/mL)

C_U = nominal concentration of ibuprofen in the *Sample solution* (mg/mL)

Calculate the percentage of any unspecified degradation product in the portion of Oral Suspension taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of any individual unspecified degradation product from the *Sample solution*

r_S = peak response of ibuprofen from *Standard solution A*

C_S = concentration of USP Ibuprofen RS in *Standard solution A* (mg/mL)

C_U = nominal concentration of ibuprofen in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*. Disregard any peaks less than 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)	
		For 20 mg/mL Strength	For 40 mg/mL Strength
Benzoic acid[a]	0.33	—	—
Ibuprofen related compound J	0.48	0.2	0.2
Ibuprofen related compound C	0.81	0.25	0.10
Ibuprofen	1.00	—	—
Any unspecified degradation product	—	0.2	0.2
Total degradation products	—	0.9	0.7

[a] Excipient, not included in the total degradation products.

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 3.6–4.6

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, and store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Benzoic Acid RS

USP Ibuprofen RS

USP Ibuprofen Related Compound C RS

4-Isobutylacetophenone.

$C_{12}H_{16}O$ 176.25

USP Ibuprofen Related Compound J RS

2-(4-Isobutyrylphenyl)propanoic acid.

$C_{13}H_{16}O_3$ 220.26

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

Topic/Question	Contact	Expert Committee
IBUPROFEN ORAL SUSPENSION	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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