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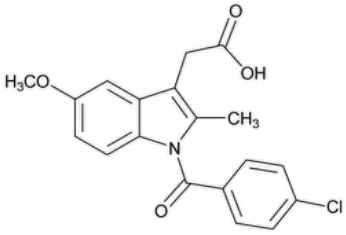
Indomethacin



$C_{19}H_{16}ClNO_4$ 357.79

1*H*-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-;

1-(*p*-Chlorobenzoyl)-5-methoxy-2-methylindole-3-acetic acid CAS RN®: 53-86-1; UNII: XXE1CET956.

DEFINITION

Indomethacin contains NLT 98.0% and NMT 102.0% of indomethacin ($C_{19}H_{16}ClNO_4$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197M▲ (CN 1-May-2020)

• **B.**

The retention time of the indomethacin peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: 0.1% formic acid

Solution B: Acetonitrile

Mobile phase: *Solution A* and *Solution B* (55:45)

Diluent: *Solution A* and *Solution B* (55:45), adjusted with 0.2 M sodium hydroxide to a pH of 8.0

System suitability solution: 2.0 mg/mL of USP Indomethacin RS, 0.002 mg/mL of USP Indomethacin Related Compound A RS, and 0.01 mg/mL of USP Indomethacin Related Compound B RS, prepared as follows. Transfer a quantity of USP Indomethacin RS to a suitable volumetric flask. Add 50% of the final volume of acetonitrile and sonicate to dissolve. Add suitable amounts of USP Indomethacin Related Compound A RS and USP Indomethacin Related Compound B RS to the resulting solution, sonicate to dissolve if necessary, and dilute with *Diluent* to volume.

Standard solution: 0.5 mg/mL of USP Indomethacin RS in *Diluent*. Sonicate to dissolve.

Sample solution: 0.5 mg/mL of Indomethacin in *Diluent*. Sonicate to dissolve.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Temperatures

Autosampler: 4°

Column: 30°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for indomethacin related compound A and indomethacin related compound B are 0.24 and 0.37, respectively.]

Suitability requirements

Resolution: NLT 2.0 between indomethacin related compound B and indomethacin related compound A, *System suitability solution*

Tailing factor: NMT 2.0 for indomethacin, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of indomethacin ($C_{19}H_{16}ClNO_4$) in the portion of Indomethacin taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.2%
- **ORGANIC IMPURITIES**

Solution A, Solution B, Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 0.002 mg/mL of USP Indomethacin RS, 0.002 mg/mL of USP Indomethacin Related Compound A RS, and 0.01 mg/mL of USP Indomethacin Related Compound B RS in *Diluent*. Sonicate to dissolve.

Sample solution: 2.0 mg/mL of Indomethacin, prepared as follows. Transfer a quantity of Indomethacin to a suitable volumetric flask. Add 50% of the final volume of acetonitrile and sonicate to dissolve. Dilute with *Diluent* to volume.

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between indomethacin related compound A and indomethacin related compound B

Tailing factor: NMT 2.0 for indomethacin related compound A, indomethacin related compound B, and indomethacin

Relative standard deviation: NMT 5.0% for indomethacin related compound A, indomethacin related compound B, and indomethacin

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of indomethacin related compound A and indomethacin related compound B in the portion of Indomethacin taken:

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

r_U = peak response of indomethacin related compound A or indomethacin related compound B from the *Sample solution*

r_S = peak response of indomethacin related compound A or indomethacin related compound B from the *Standard solution*

C_S = concentration of USP Indomethacin Related Compound A RS or USP Indomethacin Related Compound B RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any individual unspecified impurity in the portion of Indomethacin taken:

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

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

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

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

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Indomethacin related compound A	0.24	0.15
Indomethacin related compound B	0.37	0.5
Indomethacin	1.0	—
Any individual unspecified impurity	—	0.10
Total impurities	—	1.0

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry at a pressure below 5 mm of mercury at 100° for 2 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers.

• **USP Reference Standards** ⟨11⟩

USP Indomethacin RS

USP Indomethacin Related Compound A RS

(5-Methoxy-2-methylindol-3-yl)acetic acid.

$C_{12}H_{13}NO_3$ 219.24

USP Indomethacin Related Compound B RS

4-Chlorobenzoic acid.

$C_7H_5ClO_2$ 156.57

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

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

Chromatographic Database Information: Chromatographic Database

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