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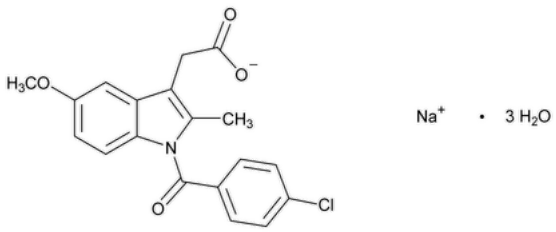
Indomethacin Sodium



$C_{19}H_{15}ClNNaO_4 \cdot 3H_2O$ 433.82

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

Sodium 1-(*p*-chlorobenzoyl)-5-methoxy-2-methylindole-3-acetate, trihydrate CAS RN®: 74252-25-8; UNII: 0IMX38M2GG.

Anhydrous 379.78

DEFINITION

Indomethacin Sodium contains NLT 98.0% and NMT 102.0% of indomethacin sodium ($C_{19}H_{15}ClNNaO_4$), calculated on the dried basis.

IDENTIFICATION

- **A.**

  Sample: A small quantity

  Analysis: Ignite the *Sample* on a platinum wire in a nonluminous flame.

  Acceptance criteria: An intense yellow flame is produced.

- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C.** The UV-Vis spectrum of the major 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 in water

  Solution B: 0.025% formic acid in acetonitrile

  Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	70	30
2	70	30
20	15	85
25	15	85
26	70	30
30	70	30

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

System suitability solution: 0.82 mg/mL of USP Indomethacin RS, 0.002 mg/mL of USP Indomethacin Related Compound A RS, and 0.002 mg/mL of USP Indomethacin Related Compound B RS in *Diluent*. Sonicate to dissolve.

Standard solution: 0.82 mg/mL of USP Indomethacin RS dissolved in a minimum quantity of acetonitrile. Dilute with *Diluent* to volume. Sonicate to dissolve.

Sample solution: 1.0 mg/mL of Indomethacin Sodium trihydrate in *Diluent*. Sonicate to dissolve.

Chromatographic system

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

Mode: LC

Detector: 240 nm. For *Identification C*, use a diode array detector in the range of 190–400 nm.

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

Column temperature: 40°

Flow rate: 1 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 0.50 and 0.67, respectively.]

Suitability requirements

Resolution: NLT 10 between indomethacin related compound A and indomethacin related compound B, *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 sodium ($C_{19}H_{15}ClNNaO_4$) in the portion of Indomethacin Sodium taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

M_{r1} = molecular weight of anhydrous indomethacin sodium, 379.78

M_{r2} = molecular weight of indomethacin, 357.79

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

IMPURITIES

• **LIMIT OF ACETONE**

Standard solution: Transfer 1.0 mL of acetone to a 100-mL volumetric flask, and dilute with water to volume. Transfer 1.0 mL of this solution to a 200-mL volumetric flask, dilute with water to volume, insert a stopper, and cool in an ice bath.

Sample solution: Transfer 100 mg of Indomethacin Sodium to a 15-mL centrifuge tube, and dissolve in 1.0 mL of cool water. While vortexing this solution, add 1.0 mL of 0.24 N hydrochloric acid, centrifuge promptly, and filter the supernatant. Collect the filtrate in a suitable tube, cap, and cool in an ice bath.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 3-mm × 1.8-m; support S3

Column temperature: 165°

Carrier gas: Nitrogen

Injection volume: 3 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Capacity factor, *k'*: 4–7 for acetone

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

[NOTE—Use the solvent flush technique, with water as the flushing agent, and record the chromatograms for 6 min.]

Calculate the percentage of acetone in the portion of Indomethacin Sodium taken:

$$\text{Result} = S_G(10/W_U)(r_U/r_S)$$

S_G = specific gravity of acetone, 0.79

W_U = quantity of Indomethacin Sodium taken to prepare the *Sample solution* (mg)

r_U = peak area of acetone from the *Sample solution*

r_S = peak area of acetone from the *Standard solution*

Acceptance criteria: NMT 0.1%

- **Organic Impurities**

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

Standard solution: 0.002 mg/mL each of USP Indomethacin RS, USP Indomethacin Related Compound A RS, and USP Indomethacin Related Compound B RS, dissolved in a minimum quantity of acetonitrile. Dilute with *Diluent* to volume. Sonicate to dissolve.

Sample solution: 1.0 mg/mL of Indomethacin Sodium in *Diluent*. Sonicate to dissolve.

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 10 between indomethacin related compound A and indomethacin related compound B

Relative standard deviation: NMT 2.5% 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 or indomethacin related compound B in the portion of Indomethacin Sodium 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 the corresponding related compound from the *Standard solution*

C_S = concentration of the corresponding USP Reference Standard in the *Standard solution* (mg/mL)

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

Calculate the percentage of any individual unspecified impurity in the portion of Indomethacin Sodium 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 Sodium in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Indomethacin related compound A	0.50	0.2[a]
Indomethacin related compound B	0.67	—
Indomethacin	1.0	—
Any individual unspecified impurity	—	0.5
Total impurities	—	1.0[b]

[a] The sum of the percentages of indomethacin related compound A and indomethacin related compound B is NMT 0.2%.

[b] Excluding the percentages for indomethacin related compound A and indomethacin related compound B.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 100° for 2 h at a pressure not exceeding 5 mm of mercury.

Acceptance criteria: 11.5%–13.5%

• **Other Requirements:** Where the label states that Indomethacin Sodium is sterile, it meets the requirements for *Sterility Tests* ⟨71⟩ and for the *Bacterial Endotoxins Test* under *Indomethacin for Injection*. Where the label states that Indomethacin Sodium must be subjected to further processing during the preparation of injectable dosage forms, it meets the requirements for the *Bacterial Endotoxins Test* under *Indomethacin for Injection*.

ADDITIONAL REQUIREMENTS

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

• **Labeling:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Indomethacin RS

USP Indomethacin Related Compound A RS

2-(5-Methoxy-2-methyl-1*H*-indol-3-yl)acetic acid.

▲$C_{12}H_{13}NO_3$▲ (ERR 1-Dec-2024) 219.24

USP Indomethacin Related Compound B RS

4-Chlorobenzoic acid.

▲$C_7H_5ClO_2$▲ (ERR 1-Dec-2024) 156.57

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

Topic/Question	Contact	Expert Committee
INDOMETHACIN SODIUM	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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