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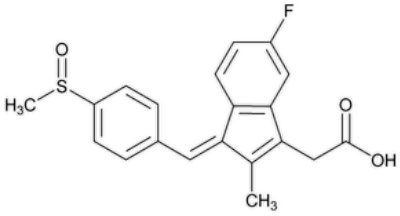
Sulindac



$C_{20}H_{17}FO_3S$ 356.41

1*H*-Indene-3-acetic acid, 5-fluoro-2-methyl-1-[[4-(methylsulfinyl) phenyl]methylene]-, (*Z*)-;

cis-5-Fluoro-2-methyl-1-[(*p*-methylsulfinyl)benzylidene]indene-3-acetic acid CAS RN®: 38194-50-2; UNII: 184SNS8VUH.

DEFINITION

Sulindac contains NLT 98.0% and NMT 102.0% of sulindac ($C_{20}H_{17}FO_3S$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

Change to read:

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

Analytical wavelength: 284 nm

Medium: Hydrochloric acid in methanol (1 in 120)

Sample solution: 15 µg/mL in *Medium*

Acceptance criteria: Absorptivities, calculated on the dried basis, do not differ by more than 3.0%.

• **C.** The retention time 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: 0.1% Formic acid in acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0.0	70	30
8.0	70	30
15.0	10	90
18.0	10	90
18.1	70	30

Time (min)	Solution A (%)	Solution B (%)
20.0	70	30

Diluent: Acetonitrile and water (50:50)

System suitability solution: 0.003 mg/mL each of USP Sulindac RS, USP Sulindac Related Compound A RS, USP Sulindac Related Compound B RS, and USP Sulindac Related Compound C RS in *Diluent*

Standard solution: 0.2 mg/mL of USP Sulindac RS in *Diluent*

Sample solution: 0.2 mg/mL of Sulindac in *Diluent*

Chromatographic system

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

Mode: LC

Detector: 330 nm

Column: 2.1-mm × 15-cm; 1.7-µm packing L1

Column temperature: 45°

Flow rate: 0.3 mL/min

Injection volume: 2 µL

System suitability

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

[NOTE—The relative retention times for sulindac related compound A, sulindac related compound B, and sulindac related compound C are 1.25, 1.34, and 1.67, respectively.]

Suitability requirements

Resolution: NLT 4.0 between sulindac and sulindac related compound A and between sulindac related compound A and sulindac related compound B, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of sulindac ($C_{20}H_{17}FO_3S$) in the portion of Sulindac taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

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

IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%
- **RESIDUAL SOLVENTS ⟨467⟩**

Solvent: Dimethylsulfoxide

Acceptance criteria: Meets the requirements except that chloroform is NMT 500 ppm

- **ORGANIC IMPURITIES**

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

Standard solution: 0.6 µg/mL of USP Sulindac RS and 3 µg/mL each of USP Sulindac Related Compound A RS, USP Sulindac Related Compound B RS, and USP Sulindac Related Compound C RS in *Diluent*. Sonicate for 2–5 min.

Sample solution: 600 µg/mL of Sulindac in *Diluent*. Sonicate for 2–5 min.

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 4.0 between sulindac and sulindac related compound A and between sulindac related compound A and sulindac related compound B

Relative standard deviation: NMT 2.0% for any peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentages of sulindac related compound A, sulindac related compound B, and sulindac related compound C in the portion of Sulindac taken:

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

r_U = peak response of the specified impurity from the *Sample solution*

r_S = peak response of the corresponding related compound from the *Standard solution*

C_S = concentration of the corresponding related compound in the *Standard solution* (µg/mL)

C_U = concentration of Sulindac in the *Sample solution* (µg/mL)

Calculate the percentage of any individual unspecified impurity in the portion of Sulindac 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 sulindac from the *Standard solution*

C_S = concentration of USP Sulindac RS in the *Standard solution* (µg/mL)

C_U = concentration of Sulindac in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Sulindac	1.0	—
Sulindac related compound A[a]	1.25	0.5
Sulindac related compound B[b]	1.34	0.5
Sulindac related compound C[c]	1.67	0.5
Any individual unspecified impurity	—	0.10
Total impurities	—	1.0

[a] (*E*)-2-{5-Fluoro-2-methyl-1-[4-(methylsulfinyl)benzylidene]-1*H*-inden-3-yl}acetic acid.

[b] (*Z*)-2-{5-Fluoro-2-methyl-1-[4-(methylsulfonyl)benzylidene]-1*H*-inden-3-yl}acetic acid.

[c] (*Z*)-2-{5-Fluoro-2-methyl-1-[4-(methylthio)benzylidene]-1*H*-inden-3-yl}acetic acid.

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry under vacuum at 100° for 2 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers.
- **USP Reference Standards** ⟨11⟩

USP Sulindac RS

USP Sulindac Related Compound A RS

(*E*)-2-{5-Fluoro-2-methyl-1-[4-(methylsulfinyl)benzylidene]-1*H*-inden-3-yl}acetic acid.

$C_{20}H_{17}FO_3S$ 356.41

USP Sulindac Related Compound B RS

(*Z*)-2-{5-Fluoro-2-methyl-1-[4-(methylsulfonyl)benzylidene]-1*H*-inden-3-yl}acetic acid.

$C_{20}H_{17}FO_4S$ 372.41

USP Sulindac Related Compound C RS

(*Z*)-2-{5-Fluoro-2-methyl-1-[4-(methylthio)benzylidene]-1*H*-inden-3-yl}acetic acid.

$C_{20}H_{17}FO_2S$ 340.41

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

Topic/Question	Contact	Expert Committee
SULINDAC	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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