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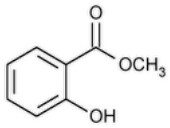
Methyl Salicylate



$C_8H_8O_3$ 152.15
Benzoic acid, 2-hydroxy-, methyl ester;
Methyl salicylate CAS RN®: 119-36-8.

DEFINITION

Methyl Salicylate is produced synthetically or is obtained by maceration and subsequent distillation with steam from the leaves of *Gaultheria procumbens* L. (Fam. Ericaceae) or from the bark of *Betula lenta* L. (Fam. Betulaceae). It contains NLT 98.0% and NMT 102.0% of methyl salicylate ($C_8H_8O_3$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197F

• **B. Chromatographic Identity**

Analysis: Proceed as directed in the *Assay*.

Acceptance criteria: The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*.

ASSAY

• **Procedure**

Mobile phase: Methanol and 0.1% phosphoric acid (55:45)

Diluent: Methanol

System suitability solution: 150 µg/mL of USP Methyl Salicylate RS and 3 µg/mL of USP Methyl Salicylate Related Compound A RS in *Diluent*

Standard solution: 150 µg/mL of USP Methyl Salicylate RS in *Diluent*

Sample solution: 150 µg/mL of Methyl Salicylate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 237 nm

Column: 4.6-mm × 7.5-cm; 3.5-µm packing L7

Column temperature: Ambient

Flow rate: 1.0 mL/min

Injection volume: 10 µL

Run time: 7 min

System suitability

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

[Note—The relative retention times for methyl salicylate and dimethyl 4-hydroxyisophthalate are 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 1.5 between the methyl salicylate and dimethyl 4-hydroxyisophthalate peaks, *System suitability solution*

Tailing factor: NMT 1.5 for the methyl salicylate peak, *Standard solution*

Relative standard deviation: NMT 0.5% for the methyl salicylate peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of methyl salicylate ($C_8H_8O_3$) in the portion of Methyl Salicylate 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 Methyl Salicylate RS in the *Standard solution* (µg/mL)

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

Acceptance criteria: 98.0%–102.0%

IMPURITIES

• **Limit of Salicylic Acid and Dimethyl 4-Hydroxyisophthalate**

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

Standard solution: 0.15 µg/mL of USP Salicylic Acid RS, 0.15 µg/mL of USP Methyl Salicylate RS, and 0.75 µg/mL of USP Methyl Salicylate Related Compound A RS in *Diluent*

System suitability

Sample: *Standard solution*

[Note—The relative retention times for salicylic acid, methyl salicylate, and dimethyl 4-hydroxyisophthalate are 0.6, 1.0, and 1.2, respectively.]

Suitability requirements

Resolution: NLT 4 between the salicylic acid and methyl salicylate peaks; NLT 2 between the methyl salicylate and dimethyl 4-hydroxyisophthalate peaks

Relative standard deviation: NMT 3% for all three peaks

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of each individual impurity in the portion of Methyl Salicylate taken:

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

r_U = peak response of salicylic acid or dimethyl 4-hydroxyisophthalate from the *Sample solution*

r_S = peak response of salicylic acid or dimethyl 4-hydroxyisophthalate from the *Standard solution*

C_S = concentration of USP Salicylic Acid RS or USP Methyl Salicylate Related Compound A RS in the *Standard solution* (µg/mL)

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

Acceptance criteria

Salicylic acid: NMT 0.1%

Dimethyl 4-hydroxyisophthalate: NMT 0.5%

SPECIFIC TESTS

• **Solubility in 70% Alcohol:** One volume of synthetic Methyl Salicylate dissolves in seven volumes of 70% alcohol. One volume of natural Methyl Salicylate dissolves in seven volumes of 70% alcohol, and the solution shows NMT a slight cloudiness.

• **Specific Gravity ⟨841⟩:** 1.180–1.185 for the synthetic variety; 1.176–1.182 for the natural variety

Change to read:

• **Optical Rotation ⟨781A⟩**, *Procedures, Angular Rotation*

▲[Note—This test is not required for synthetic Methyl Salicylate or that from *Betula lenta*.]▲ (NF 1-Dec-2021)

Methyl Salicylate from *Gaultheria procumbens* is slightly levorotatory, with the angular rotation not exceeding −1.5° in a 100-mm tube.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **Labeling:** Label it to indicate whether it was made synthetically or distilled from either of the plants of *Gaultheria procumbens* or *Betula lenta*.

• **USP Reference Standards ⟨11⟩**

USP Methyl Salicylate RS

USP Methyl Salicylate Related Compound A RS

Dimethyl 4-hydroxyisophthalate.

$C_{10}H_{10}O_5$ 210.18

USP Salicylic Acid RS

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

Topic/Question	Contact	Expert Committee
METHYL SALICYLATE	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 46(3)

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