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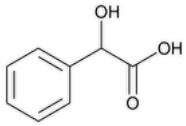
# Mandelic Acid



$C_8H_8O_3$ 152.15
Benzeneacetic acid, α-hydroxy-;
(*RS*)-2-Hydroxy-2-phenylacetic acid;
(±)-α-Hydroxyphenylacetic acid;
2-Hydroxy-2-phenylacetic acid CAS RN®: 90-64-2.

## DEFINITION

Mandelic Acid contains NLT 98.0% and NMT 102.0% of α-hydroxyphenylacetic acid ($C_8H_8O_3$), calculated on the anhydrous basis.

## IDENTIFICATION

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

• **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*, as obtained in the *Assay*.

## ASSAY

• **Procedure**

**Solvent A:** 0.01 M phosphoric acid

**Mobile phase:** Acetonitrile, methanol, and *Solvent A* (17:3:80)

**Standard stock solution A:** Prepare a solution having known concentrations of 0.2 mg/mL of acetophenone, 0.5 mg/mL of benzoylformic acid, and 0.25 mg/mL of USP Benzaldehyde RS, respectively, in *Mobile phase*.

**Standard stock solution B:** Transfer 25 mg of USP Benzoic Acid RS to a 250-mL volumetric flask, add 5.0 mL of *Standard stock solution A*, dilute with *Mobile phase* to volume, and mix.

**Standard stock solution C:** Use USP Mandelic Acid RS to prepare a solution having a known concentration of 5 mg/mL in *Mobile phase*.

**System suitability solution:** Transfer 5.0 mL of *Standard stock solution B* and 20.0 mL of *Standard stock solution C* to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. The solution contains 1 mg/mL of USP Mandelic Acid RS, 0.2 µg/mL of acetophenone, 0.5 µg/mL of benzoylformic acid, 0.25 µg/mL of USP Benzaldehyde RS, and 5 µg/mL of USP Benzoic Acid RS.

**Standard solution:** 1 mg/mL of USP Mandelic Acid RS in *Mobile phase* prepared from *Standard stock solution C*

**Sample solution:** 1 mg/mL of Mandelic Acid in *Mobile phase*

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 240 nm

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

**Column temperature:** Ambient

**Flow rate:** 0.8 mL/min

**Injection volume:** 20 µL

**System suitability**

**Sample:** *System suitability solution*

[Note—See *Table 1* for relative retention times.]

**Table 1**

| Component | Relative Retention Time |
|---|---|
| Benzoylformic acid | 0.9 |
| Mandelic acid | 1.0 |
| Benzoic acid | 3.2 |
| Benzaldehyde | 3.6 |
| Acetophenone | 4.8 |

**Suitability requirements**

**Resolution:** NLT 3.0, between the benzoylformic acid peak and the mandelic acid peak and between the benzoic acid peak and the benzaldehyde peak

**Relative standard deviation:** NMT 1% for the mandelic acid peak

**Tailing factor:** NMT 2.0 for each peak

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of mandelic acid ($C_8H_8O_3$) in the portion of Mandelic Acid taken:

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

$r_U$ = peak response of mandelic acid from the *Sample solution*

$r_S$ = peak response of mandelic acid from the *Standard solution*

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

$C_U$ = concentration of Mandelic Acid in the *Sample solution* (mg/mL)

**Acceptance criteria:** 98.0%–102.0% on the anhydrous basis

## IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Limit of Benzoylformic Acid, Benzaldehyde, Benzoic Acid, and Acetophenone**

**Standard stock solution A, Standard stock solution B, Chromatographic system,** and **System suitability:** Proceed as directed in the *Assay*.

**Standard solution:** Transfer 5.0 mL of *Standard stock solution B* to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. The *Standard solution* contains 0.2 µg/mL of acetophenone, 0.5 µg/mL of benzoylformic acid, 0.25 µg/mL of USP Benzaldehyde RS, and 5 µg/mL of USP Benzoic Acid RS.

**Sample solution:** 2.5 mg/mL of Mandelic Acid in *Mobile phase*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of each related compound (benzoylformic acid, benzaldehyde, benzoic acid, or acetophenone) in the portion of Mandelic Acid taken:

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

$r_U$ = peak response of the relevant related compound (benzoylformic acid, benzaldehyde, benzoic acid, or acetophenone) from the *Sample solution*

$r_S$ = peak response of the relevant related compound (benzoylformic acid, benzaldehyde, benzoic acid, or acetophenone) from the *Standard solution*

$C_S$ = concentration of the relevant related compound (benzoylformic acid, USP Benzaldehyde RS, USP Benzoic Acid RS, or acetophenone) in the *Standard solution* (mg/mL)

$C_U$ = concentration of Mandelic Acid in the *Sample solution* (mg/mL)

**Acceptance criteria**

**Benzoylformic acid:** NMT 0.1%

**Benzoic acid:** NMT 1.0%

**Benzaldehyde:** NMT 0.05%

**Acetophenone:** NMT 0.01%

• **Limit of Chloride**

**Sample:** 1 g

**Analysis:** Proceed as directed for *Chloride and Sulfate ⟨221⟩, Chloride*.

**Acceptance criteria:** 0.01%; a 1-g portion shows no more than corresponds to 0.15 mL of 0.020 N hydrochloric acid.

## SPECIFIC TESTS

• **Melting Range or Temperature ⟨741⟩:** 118°–121°

• **Water Determination, *Method Ia* ⟨921⟩:** NMT 0.5%

***Change to read:***

• **Turbidity**

(See *Nephelometry and Turbidimetry ⟨855⟩*.)

**Sample solution:** 50 mg/mL in water

**Blank:** Reserve a portion of the water used to prepare the *Sample solution*.

**Fixed reproducible standards:** See *Determination of Turbidity* in ▲*Elastomeric Components Used in Injectable Pharmaceutical Packaging/Delivery Systems ⟨381⟩*▲ (CN 1-Dec-2020) ·

**Analysis:** Measure the turbidity of the *Sample solution* and *Blank* as directed in *Nephelometry and Turbidimetry ⟨855⟩* against the *Fixed reproducible standards*.

**Acceptance criteria:** The turbidity is the difference between the values obtained for the *Blank* and the *Sample solution*, expressed in Nephelos units. The *Sample solution* shows no more turbidity than the 10 Nephelos units standard.

## ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store in a dry and well-ventilated place. Protect from light.

• **USP Reference Standards ⟨11⟩**

USP Benzaldehyde RS
USP Benzoic Acid RS
USP Mandelic Acid RS

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| MANDELIC ACID | Documentary Standards Support | SE2020 Simple Excipients |

**Chromatographic Database Information:** Chromatographic Database

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