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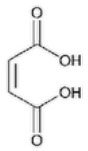
# Maleic Acid



$C_4H_4O_4$ 116.07

(*Z*)-Butenedioic acid;

*cis*-Butenedioic acid CAS RN®: 110-16-7.

## DEFINITION

Maleic Acid contains NLT 98.0% and NMT 102.0% of maleic acid ($C_4H_4O_4$), calculated on the anhydrous basis.

## IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**
- **B.** The retention time of the maleic acid peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

## ASSAY

- **Procedure**

**Solution A:** 10 mM potassium phosphate buffer, adjusted with phosphoric acid to a pH of 2.3

**Solution B:** Acetonitrile and *Solution A* (55:45)

**Mobile phase:** See *Table 1*.

**Table 1**

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 0.0 | 99 | 1 |
| 8.0 | 95 | 5 |
| 22.0 | 55 | 45 |
| 27.0 | 55 | 45 |

Return to original conditions and re-equilibrate the system.

**Diluent:** Acetonitrile and *Solution A* (2:98)

**System suitability solution:** 50 µg/mL of USP Fumaric Acid RS and 200 µg/mL each of USP Lactic Acid RS, USP Glacial Acetic Acid RS, and USP Succinic Acid RS in *Diluent*

**Standard solution:** 50 µg/mL of USP Maleic Acid RS in *Diluent*

**Sample solution:** 50 µg/mL of Maleic Acid in *Diluent*

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 210 nm

**Column:** 4.6-mm × 15-cm; 3-µm packing L1

**Flow rate:** 0.8 mL/min

**Injection volume:** 10 µL

**System suitability**

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

[Note—The relative retention times for lactic acid, acetic acid, succinic acid, and fumaric acid are about 0.5, 0.6, 0.9, and 1.0, respectively.]

**Suitability requirements**

**Resolution:** NLT 2.0 between the lactic acid and acetic acid peaks; NLT 3.0 between the succinic acid and fumaric acid peaks, *System suitability solution*

**Tailing factor:** NMT 1.5, *Standard solution*

**Relative standard deviation:** NMT 1.0%, *Standard solution*

**Analysis**

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

Calculate the percentage of maleic acid in the portion of Maleic Acid taken:

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

$r_U$ = peak area of maleic acid from the *Sample solution*

$r_S$ = peak area of maleic acid from the *Standard solution*

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

$C_U$ = concentration of Maleic Acid in the *Sample solution* (µg/mL)

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

## IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%, determined on a 1.0-g portion

***Change to read:***

• **Limit of Iron**

**Solution A:** Dissolve 9.7 g of potassium thiocyanate in 100 mL of water.

**Diluted standard iron solution:** Immediately before use, dilute 1 volume of *Standard Iron Solution*, prepared as directed in ▲*Iron ⟨241⟩, Procedures, Procedure 1*▲ (CN 1-Jun-2023), with 9 volumes of water. [Note—This solution contains the equivalent of 1 µg/mL of iron.]

**Standard solution:** Add 6 mL of water to 5 mL of *Diluted standard iron solution*. Add 1 mL of diluted hydrochloric acid and 0.05 mL of bromine TS. After 5 min, remove the excess of bromine with the aid of a current of air, add 3 mL of *Solution A*, and shake well.

**Sample solution:** Dissolve 1 g of Maleic Acid in 10 mL of water. Add 2 mL of diluted hydrochloric acid and 0.05 mL of bromine TS. After 5 min, remove the excess of bromine with the aid of a current of air, add 3 mL of *Solution A*, and shake well.

**Analysis:** Allow the *Standard solution* and *Sample solution* to stand for 5 min.

**Acceptance criteria:** Any red color in the *Sample solution* is not more intense than that in the *Standard solution* (NMT 5 ppm).

• **Limit of Fumaric Acid and Malic Acid**

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

**Standard solution:** 50 µg/mL of USP Fumaric Acid RS and 25 µg/mL of USP Malic Acid RS

**Sample solution:** 5 mg/mL of Maleic Acid in *Diluent*

**System suitability**

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

[Note—The relative retention times for lactic acid, acetic acid, succinic acid, and fumaric acid are about 0.5, 0.6, 0.9, and 1.0, respectively.]

**Suitability requirements**

**Resolution:** NLT 2.0 between the lactic acid and acetic acid peaks; NLT 3.0 between the succinic acid and fumaric acid peaks, *System suitability solution*

**Tailing factor:** NMT 1.5 for malic acid and fumaric acid, *Standard solution*

**Relative standard deviation:** NMT 3.0% for the malic acid and fumaric acid peaks, *Standard solution*

**Analysis**

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

Calculate the percentage of fumaric acid or malic acid in the portion of Maleic Acid taken:

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

$r_U$ = peak area of fumaric acid or malic acid from the *Sample solution*

$r_S$ = peak area of fumaric acid or malic acid from the *Standard solution*

$C_S$ = concentration of USP Fumaric Acid RS or USP Malic Acid RS in the *Standard solution* (µg/mL)

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

$F$ = conversion factor, 0.001 mg/µg

**Acceptance criteria**

**Fumaric acid:** NMT 1.0%

**Malic acid:** NMT 0.5%

### SPECIFIC TESTS

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

### ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight glass containers, protected from light. Store at room temperature.

• **Labeling:** Where Maleic Acid is intended for use in the manufacture of injectable dosage forms, it is so labeled. Where Maleic Acid must be subjected to further processing during the preparation of injectable dosage forms to ensure acceptable levels of bacterial endotoxins, it is so labeled.

• **USP Reference Standards ⟨11⟩**

USP Fumaric Acid RS
USP Glacial Acetic Acid RS
USP Lactic Acid RS
USP Maleic Acid RS
USP Malic Acid RS
USP Succinic Acid RS

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| MALEIC ACID | Documentary Standards Support | SE2020 Simple Excipients |
| REFERENCE STANDARD SUPPORT | RS Technical Services<br>RSTECH@usp.org | SE2020 Simple Excipients |

**Chromatographic Database Information:** Chromatographic Database

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