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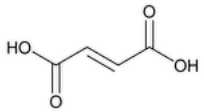
Fumaric Acid



$C_4H_4O_4$ 116.07

2-Butenedioic acid, *E*-;

Fumaric acid CAS RN®: 110-17-8.

Change to read:

DEFINITION

Fumaric Acid contains ▲NLT 98.0% and NMT 102.0% of fumaric acid▲ (NF 1-Dec-2022) of ($C_4H_4O_4$), calculated on the anhydrous basis.

IDENTIFICATION

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

Add the following:

▲• **B. Chromatographic Identity:** The retention time of the fumaric acid peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (NF 1-Dec-2022)

Change to read:

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 starting 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 Glacial Acetic Acid RS, USP Lactic Acid RS, and USP Succinic Acid RS in *Diluent*

Standard solution: 50 µg/mL of USP Fumaric Acid RS in *Diluent*. Sonicate, if necessary.

Sample solution: 50 µg/mL of Fumaric Acid in *Diluent*. Sonicate, if necessary.

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 0.51, 0.54, 0.91, 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 fumaric acid ($C_4H_4O_4$) in the portion of Fumaric Acid taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the anhydrous basis▲ (NF 1-Dec-2022)

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%

Change to read:

• **LIMIT OF MALEIC ACID ▲AND MALIC ACID**

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

System suitability solution: 25 µg/mL of USP Fumaric Acid RS and 100 µg/mL each of USP Glacial Acetic Acid RS, USP Lactic Acid RS, and USP Succinic Acid RS in *Diluent* prepared by diluting the *System suitability solution* described in the *Assay* with *Diluent* in half.

Standard solution: 2.5 µg/mL of USP Maleic Acid RS and 37.5 µg/mL of USP Malic Acid RS

Sample solution: 2.5 mg/mL of Fumaric Acid in *Diluent*, prepared as follows. To a volumetric flask containing an accurately weighed amount of Fumaric Acid, add *Diluent* up to about 80% of the flask volume, sonicate the content at 35° for 30 min, cool to room temperature, and dilute with *Diluent* to volume. Vortex, if necessary.

Chromatographic system: Proceed as directed in the *Assay*, except for the *Injection volume*.

Injection volume: 20 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 0.51, 0.54, 0.91, 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 maleic acid and malic acid, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of maleic acid or malic acid in the portion of Fumaric Acid taken:

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

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

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

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

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

F = conversion factor, 0.001 mg/µg

Acceptance criteria

Maleic acid: NMT 0.1%

Malic acid: NMT 1.5%▲ (NF 1-Dec-2022)

SPECIFIC TESTS

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

ADDITIONAL REQUIREMENTS

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

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Fumaric Acid RS

▲USP Glacial Acetic Acid RS

USP Lactic Acid RS▲ (NF 1-Dec-2022)

USP Maleic Acid RS

▲USP Malic Acid RS

USP Succinic Acid RS▲ (NF 1-Dec-2022)

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

Topic/Question	Contact	Expert Committee
FUMARIC ACID	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

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