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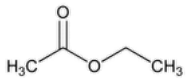
Ethyl Acetate



$C_4H_8O_2$ 88.11

Acetic acid, ethyl ester;

Ethyl acetate CAS RN®: 141-78-6.

DEFINITION

Ethyl Acetate contains NLT 98.0% and NMT 102.0% of ethyl acetate ($C_4H_8O_2$).

IDENTIFICATION

Change to read:

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

ASSAY

• **Procedure**

Diluent: *N,N*-dimethylacetamide

System suitability solution: 2.0 mg/mL of USP Ethyl Acetate RS and 20 µg/mL of USP Methyl Ethyl Ketone RS in *Diluent*

Standard solution: 2.0 mg/mL of USP Ethyl Acetate RS in *Diluent*

Sample solution: 2.0 mg/mL of Ethyl Acetate in *Diluent*

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 60-m; coated with a 1.8-µm film of phase G43

Temperatures

Detector: 250°

Injection port: 210°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	—	40	15
40	12	200	2

Carrier gas: Helium

Flow rate: 3.0 mL/min

Injection volume: 1 µL

Injection type: Split injection, split ratio 30:1

Run time: 30.3 min

System suitability

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

[Note—The relative retention times for methyl ethyl ketone and ethyl acetate are 0.97 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between the methyl ethyl ketone and ethyl acetate peaks, *System suitability solution*

Tailing factor: NMT 1.5 for the ethyl acetate peak, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ethyl acetate ($C_4H_8O_2$) in the portion of Ethyl Acetate taken:

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

r_U = peak area of ethyl acetate from the *Sample solution*

r_S = peak area of ethyl acetate from the *Standard solution*

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

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

P = labeled purity of USP Ethyl Acetate RS

Acceptance criteria: 98.0%–102.0%

IMPURITIES

• **Limit of Nonvolatile Residue**

Sample: Ethyl Acetate

Analysis: Evaporate the *Sample* in a tared porcelain dish on a steam bath, and dry at 105° for 1 h.

Acceptance criteria: NMT 0.02%

Change to read:

• **Chromatographic Purity**

Diluent and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 0.16 mg/mL each of acetaldehyde and methanol, 160 mg/mL of Ethyl Acetate, and 1.6 mg/mL of USP Methyl Ethyl Ketone RS in *Diluent*

Sensitivity solution: 0.08 mg/mL each of acetaldehyde, USP Ethyl Acetate RS, and USP 1-Ethoxy-2-methylpropane RS in *Diluent*

Methyl compounds identification solution: 0.16 mg/mL each of methanol, methyl acetate, and methyl isobutyrate in *Diluent*

Standard solution: 0.16 mg/mL each of acetaldehyde, USP Ethyl Acetate RS, and USP 1-Ethoxy-2-methylpropane RS in *Diluent*

Sample solution: 160 mg/mL of Ethyl Acetate in *Diluent*

System suitability

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

[Note—The relative retention times for acetaldehyde, methanol, methyl ethyl ketone, ethyl acetate, and 1-ethoxy-2-methylpropane are 0.29, 0.31, 0.97, 1.0, and 1.1, respectively.]

Suitability requirements

Resolution: NLT 2.0 between the acetaldehyde and methanol peaks; NLT 2.0 between the methyl ethyl ketone and ethyl acetate peaks, *System suitability solution*

Signal-to-noise ratio: NLT 20 for the acetaldehyde, ethyl acetate, and 1-ethoxy-2-methylpropane peaks, *Sensitivity solution*

Tailing factor: NMT 1.5 for the acetaldehyde, ethyl acetate, and 1-ethoxy-2-methylpropane peaks, *Standard solution*

Relative standard deviation: NMT 5.0% for acetaldehyde, ethyl acetate, and 1-ethoxy-2-methylpropane, *Standard solution*

Analysis

Samples: *Methyl compounds identification solution*, *Standard solution*, and *Sample solution*

Calculate the percentage of acetaldehyde and 1-ethoxy-2-methylpropane in the portion of Ethyl Acetate taken:

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

r_U = peak area of acetaldehyde or 1-ethoxy-2-methylpropane from the *Sample solution*

r_S = peak area of acetaldehyde or 1-ethoxy-2-methylpropane from the *Standard solution*

C_S = concentration of acetaldehyde or USP 1-Ethoxy-2-methylpropane RS in the *Standard solution* (mg/mL)

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

Identify the methanol, methyl acetate, and methyl isobutyrate peaks in the *Sample solution* based on those in the *Methyl compounds identification solution*.

Calculate the content of methyl compounds in the portion of Ethyl Acetate taken:

$$\text{Result} = (r_T/r_S) \times F$$

r_T = sum of the peak areas of methanol, methyl acetate, and methyl isobutyrate from the *Sample solution*

r_S = peak area of ethyl acetate from the *Standard solution*

F = limit of methyl compounds, in percentage, 0.1

Acceptance criteria

Acetaldehyde: NMT 0.1%

▲1-Ethoxy-2-methylpropane:▲ (ERR 1-May-2018) NMT 0.1%

Methyl compounds: NMT 0.1%

Other impurities: NMT 0.3%; the sum of all other peaks areas in the chromatogram of the *Sample solution*, excluding the ethyl acetate, specified impurities, and solvent peaks areas, is not greater than three times the ethyl acetate peak area of the *Standard solution*.

SPECIFIC TESTS

• **Acidity**

Sample solution: 2.0 mL of Ethyl Acetate in 10 mL of neutralized alcohol

Analysis: Add 2 drops of phenolphthalein TS to the *Sample solution*. Neutralize with 0.10 N sodium hydroxide.

Acceptance criteria: NMT 0.10 mL of 0.10 N sodium hydroxide is required.

• **Readily Carbonizable Substances Test** ⟨271⟩

Sample: 2 mL of Ethyl Acetate

Analysis: Add the *Sample* carefully to 10 mL of sulfuric acid to form separate layers.

Acceptance criteria: No dark zone is developed within 15 min.

• **Specific Gravity** ⟨841⟩**:** 0.894–0.898

• **Bacterial Endotoxins Test** ⟨85⟩**:** If labeled for use in preparing parenteral dosage forms, it also meets the following requirements. The level of bacterial endotoxins is such that the requirement in the relevant dosage form monographs(s) in which Ethyl Acetate is used can be met. Where the label states that Ethyl Acetate must be subjected to further processing during the preparation of injectable dosage forms, the level of bacterial endotoxins is such that the requirement in the relevant dosage form monograph(s) in which Ethyl Acetate is used can be met.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and avoid exposure to excessive heat.

• **Labeling:** Where Ethyl Acetate is intended for use in the manufacture of injectable dosage forms, it is so labeled. Where Ethyl Acetate 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 Ethyl Acetate RS

USP 1-Ethoxy-2-methylpropane RS

USP Methyl Ethyl Ketone RS

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

Topic/Question	Contact	Expert Committee
ETHYL ACETATE	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

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