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Alcohol

Portions of this monograph that are national *USP* text, and are not part of the harmonized text, are marked with symbols (◆ ◆) to specify this fact.

C_2H_6O 46.07
Ethanol;
Ethyl alcohol CAS RN®: 64-17-5.

DEFINITION

◆Alcohol contains NLT 92.3% and NMT 93.8%, by weight, corresponding to NLT 94.9% and NMT 96.0%, by volume, at 15.56°, of ethanol (C_2H_5OH).◆

IDENTIFICATION

- **A.** It meets the requirements of the test for *Specific Gravity ⟨841⟩*.
- **B. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197F or 197S: Neat
- ◆**C. Limit of Methanol**

[Note—This test must be performed to be in compliance with USP, in addition to *Identification A* and *B* above.]

Sample solution A, Standard solution A, Standard solution B, Chromatographic system, and **System suitability:** Proceed as directed in *Organic Impurities*.

Analysis: Proceed as directed in the *Organic Impurities* test, *Methanol calculation*.

Acceptance criteria: Meets the requirements in *Table 2* for methanol.◆

IMPURITIES

- **Limit of Nonvolatile Residue**

Sample: 100 mL of Alcohol

Analysis: Evaporate the *Sample* in a tared dish on a water bath, and dry at 100°–105° for 1 h.

Acceptance criteria: The weight of the residue is NMT 2.5 mg.

- **Organic Impurities**

Sample solution A: Alcohol (substance under test)

Sample solution B: 300 µL/L of 4-methylpentan-2-ol in *Sample solution A*

Standard solution A: 200 µL/L of methanol in *Sample solution A*

◆[Note—To be prepared for use in *Identification C*]◆

Standard solution B: 10 µL/L each of methanol and acetaldehyde in *Sample solution A*

Standard solution C: 30 µL/L of acetal in *Sample solution A*

Standard solution D: 2 µL/L of benzene in *Sample solution A*

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 30-m fused-silica capillary; bonded with a 1.8-µm layer of phase G43

Injection type: Split; split ratio 20:1

Temperatures

Injection port: 200°

Detector: 280°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	0	40	12
40	10	240	10

Linear velocity: 35 cm/s

Carrier gas: Helium

Injection volume: 1.0 µL

System suitability

Sample: *Standard solution B*

Suitability requirements

Resolution: NLT 1.5 between the first major peak (acetaldehyde) and the second major peak (methanol)

Analysis

Samples: *Sample solution A*, *Sample solution B*, *Standard solution A*, *Standard solution B*, *Standard solution C*, and *Standard solution D*

Methanol calculation

◆[NOTE—To be performed as a part of *Identification C*.]◆

$$\text{Result} = (r_U/r_S)$$

r_U = peak area of methanol from *Sample solution A*

r_S = peak area of methanol from *Standard solution A*

Acetaldehyde calculation (sum of acetaldehyde and acetal)

$$\text{Result} = \{[A_E/(A_T - A_E)] \times C_A\} + \{[D_E/(D_T - D_E)] \times C_D \times (M_{r1}/M_{r2})\}$$

A_E = peak area of acetaldehyde from *Sample solution A*

A_T = peak area of acetaldehyde from *Standard solution B*

C_A = concentration of acetaldehyde in *Standard solution B* (µL/L)

D_E = peak area of acetal from *Sample solution A*

D_T = peak area of acetal from *Standard solution C*

C_D = concentration of acetal in *Standard solution C* (µL/L)

M_{r1} = molecular weight of acetaldehyde, 44.05

M_{r2} = molecular weight of acetal, 118.2

Benzene calculation

$$\text{Result} = [B_E/(B_T - B_E)] \times C_B$$

B_E = peak area of benzene from *Sample solution A*

B_T = peak area of benzene from *Standard solution D*

C_B = concentration of benzene in *Standard solution D* (µL/L)

[NOTE—If necessary, the identity of benzene can be confirmed using another suitable chromatographic system (stationary phase with a different polarity).]

Any other impurity calculation

$$\text{Result} = (r_U/r_M) \times C_M$$

r_U = peak area of each impurity in *Sample solution B*

r_M = peak area of 4-methylpentan-2-ol in *Sample solution B*

C_M = concentration of 4-methylpentan-2-ol in *Sample solution B* (µL/L)

Acceptance criteria: See *Table 2*.

Table 2

Name	Acceptance Criteria
Methanol	NMT 0.5, corresponding to 200 µL/L
Acetaldehyde and acetal	NMT 10 µL/L, expressed as acetaldehyde
Benzene	NMT 2 µL/L
Sum of all other impurities[a]	NMT 300 µL/L

[a] Disregard any peaks of less than 9 µL/L (0.03 times the area of the peak corresponding to 4-methylpentan-2-ol in *Sample solution B*).

SPECIFIC TESTS

Change to read:

• ◆**Specific Gravity ⟨841⟩:** 0.812–0.816 at 15.56°, indicating 92.3%–93.8%, by weight, or 94.9%–96.0%, by volume, of ethanol (C_2H_5OH)

▲[Note—In the event that a temperature of 15.56° cannot be reached, the *Alcoholometric Table* found in the *Reagents and Reference Tables* section of *USP-NF* can be used to provide the conversion factors needed to complete this test at other temperatures.◆]▲ (USP 1-Dec-2021)

• **Ultraviolet Absorption**

Analytical wavelength: 235–340 nm

Cell: 5 cm

Reference: Water

Acceptance criteria

Absorbance: NMT 0.40 at 240 nm; NMT 0.30 between 250 nm and 260 nm; NMT 0.10 between 270 nm and 340 nm

Curve: The spectrum shows a steadily descending curve with no observable peaks or shoulders.

• ◆**Clarity of Solution**

[Note—Compare each *Sample solution* to *Standard suspension A* and to water in diffused daylight 5 min after preparation of *Standard suspension A*.]

Hydrazine solution: 10 mg/mL of hydrazine sulfate in water. Allow to stand for 4–6 h.

Methenamine solution: Transfer 2.5 g of methenamine to a 100-mL glass-stopper flask, add 25.0 mL of water, insert the glass stopper, and mix to dissolve.

Primary opalescence suspension: Transfer 25.0 mL of *Hydrazine solution* to the *Methenamine solution* in the 100-mL glass-stopper flask. Mix, and allow to stand for 24 h. This suspension is stable for 2 months, provided it is stored in a glass container free from surface defects. The suspension must not adhere to the glass and must be well mixed before use.

Opalescence standard: Transfer 15.0 mL of the *Primary opalescence suspension* to a 1000-mL volumetric flask, and dilute with water to volume. This suspension should not be used beyond 24 h after preparation.

Standard suspension A: *Opalescence standard* and water (1 in 20)

Standard suspension B: *Opalescence standard* and water (1 in 10)

Sample solution A: Substance to be examined

Sample solution B: Dilute 1.0 mL of *Sample solution A* with water to 20 mL, and allow to stand for 5 min before testing.

Blank: Water

Analysis

Samples: *Standard suspension A*, *Standard suspension B*, *Sample solution A*, *Sample solution B*, and *Blank*

Transfer a sufficient portion of *Sample solution A* and *Sample solution B* to separate test tubes of colorless, transparent, neutral glass with a flat base and an internal diameter of 15–25 mm to obtain a depth of 40 mm. Similarly transfer portions of *Standard suspension A*, *Standard suspension B*, and *Blank* to separate matching test tubes. Compare the *Samples* in diffused daylight, viewing vertically against a black background (see *Visual Comparison ⟨630⟩*). The diffusion of light must be such that *Standard suspension A* can readily be distinguished from water, and *Standard suspension B* can readily be distinguished from *Standard suspension A*.

Acceptance criteria: *Sample solution A* and *Sample solution B* show the same clarity as that of water or their opalescence is not more pronounced than that of *Standard suspension A*.◆

• **Acidity or Alkalinity**

Phenolphthalein solution: Dissolve 0.1 g of phenolphthalein in 80 mL of alcohol, and dilute with water to 100 mL.

Sample: 20 mL of Alcohol

Analysis: To the *Sample* add 20 mL of freshly boiled and cooled water and 0.1 mL of *Phenolphthalein solution*. The solution is colorless. Add 1.0 mL of 0.01 N sodium hydroxide.

Acceptance criteria: The solution is pink (30 µL/L, expressed as acetic acid).

• ◆**Color of Solution**

Standard stock solution: Combine 3.0 mL of ferric chloride CS, 3.0 mL of cobaltous chloride CS, 2.4 mL of cupric sulfate CS, and 1.6 mL of dilute hydrochloric acid (10 mg/mL).

Standard solution: Transfer 1.0 mL of *Standard stock solution* to a 100-mL volumetric flask, and dilute with dilute hydrochloric acid (10 mg/mL). Prepare the *Standard solution* immediately before use.

Sample solution: Substance under test

Blank: Water

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Transfer a sufficient portion of the *Sample solution* to a test tube of colorless, transparent, neutral glass with a flat base and an internal diameter of 15–25 mm to obtain a depth of 40 mm. Similarly transfer portions of the *Standard solution* and *Blank* to separate, matching test tubes. Compare the *Samples* in diffused daylight, viewing vertically against a white background (see *Visual Comparison* ⟨630⟩).

Acceptance criteria: The *Sample solution* has the appearance of water or is not more intensely colored than the *Standard solution*.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, protected from light.
- **USP Reference Standards** ⟨11⟩
  USP Alcohol RS

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

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

Chromatographic Database Information: Chromatographic Database

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