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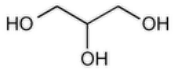
Glycerin



$C_3H_8O_3$ 92.09

1,2,3-Propanetriol;

Glycerol CAS RN®: 56-81-5.

DEFINITION

Glycerin contains NLT 99.0% and NMT 101.0% of $C_3H_8O_3$, calculated on the anhydrous basis.

IDENTIFICATION

[Note—Compliance is determined by meeting the requirements for *Identification* tests *A, B,* and *C*.]

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197F**
- **B. Limit of Diethylene Glycol and Ethylene Glycol**

Standard solution: 2.0 mg/mL of USP Glycerin RS, 0.050 mg/mL of USP Ethylene Glycol RS, 0.050 mg/mL of USP Diethylene Glycol RS, and 0.10 mg/mL of 2,2,2-trichloroethanol (internal standard) in methanol

Sample solution: 50 mg/mL of Glycerin and 0.10 mg/mL of 2,2,2-trichloroethanol (internal standard) in methanol

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 30-m fused-silica analytical column coated with 3.0-µm G43 stationary phase, and a deactivated split liner with glass wool

Temperature

Injector: 220°

Detector: 250°

Column: See the temperature program table.

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
100	—	100	4
100	50	120	10
120	50	220	6

Carrier gas: Helium

Injection size: 1.0 µL

Flow rate: 4.5 mL/min

Injection type: Split ratio, about 10:1

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for ethylene glycol, 2,2,2-trichloroethanol, diethylene glycol, and glycerin are about 0.3, 0.6, 0.8 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between diethylene glycol and glycerin

Analysis

Sample: *Sample solution*

Acceptance criteria: If a peak at the retention times for the diethylene glycol or ethylene glycol is present in the *Sample solution,* the peak response ratio relative to 2,2,2-trichloroethanol is NMT the peak response ratio for diethylene glycol or ethylene glycol relative to 2,2,2-trichloroethanol in the *Standard solution;* NMT 0.10% each for diethylene glycol and ethylene glycol is found.

• **C.** Examine the chromatograms obtained in *Identification* test *B*. The retention time of the glycerin peak of the *Sample solution* corresponds to that obtained in the *Standard solution*.

ASSAY

• **PROCEDURE**

Sodium periodate solution: Dissolve 60 g of sodium metaperiodate in sufficient water containing 120 mL of 0.1 N sulfuric acid to make 1000 mL. Do not heat to dissolve the periodate. If the solution is not clear, pass through a sintered-glass filter. Store the solution in a glass-stoppered, light-resistant container. Test the suitability of this solution as follows. Pipet 10 mL into a 250-mL volumetric flask, and dilute with water to volume. To 550 mg of Glycerin dissolved in 50 mL of water, add 50 mL of the diluted periodate solution with a pipet. For a blank, pipet 50 mL of the solution into a flask containing 50 mL of water. Allow the solutions to stand for 30 min, then to each add 5 mL of hydrochloric acid and 10 mL of potassium iodide TS, and rotate to mix. Allow to stand for 5 min, add 100 mL of water, and titrate with 0.1 N sodium thiosulfate, shaking continuously and adding 3 mL of starch TS as the endpoint is approached. The ratio of the volume of 0.1 N sodium thiosulfate required for the glycerin–periodate mixture to that required for the blank should be between 0.750 and 0.765.

Analysis: Transfer 400 mg of Glycerin to a 600-mL beaker, dilute with 50 mL of water, add bromothymol blue TS, and acidify with 0.2 N sulfuric acid to a definite green or greenish yellow color. Neutralize with 0.05 N sodium hydroxide to a definite blue endpoint, free from green color. Prepare a blank containing 50 mL of water, and neutralize in the same manner. Pipet 50 mL of the *Sodium periodate solution* into each beaker, mix by swirling gently, cover with a watch glass, and allow to stand for 30 min at room temperature (not exceeding 35°) in the dark or in subdued light. Add 10 mL of a mixture of equal volumes of ethylene glycol and water, and allow to stand for 20 min. Dilute each solution with water to 300 mL, and titrate with 0.1 N sodium hydroxide VS to a pH of 8.1 ± 0.1 for the specimen under assay and 6.5 ± 0.1 for the blank, using a pH meter. Each mL of 0.1 N sodium hydroxide, after correction for the blank, is equivalent to 9.210 mg of $C_3H_8O_3$.

Acceptance criteria: 99.0%–101.0% on the anhydrous basis

Change to read:

IMPURITIES

INORGANIC IMPURITIES

• **CHLORIDE AND SULFATE,** *Chloride*⟨221⟩**:** A 7.0-g portion shows no more chloride than corresponds to 0.10 mL of 0.020 N hydrochloric acid (NMT 10 ppm).

• **CHLORIDE AND SULFATE,** *Sulfate*⟨221⟩**:** A 10-g portion shows no more sulfate than corresponds to 0.20 mL of 0.020 N sulfuric acid (NMT 20 ppm).

• **RESIDUE ON IGNITION** ⟨281⟩**:** Heat 50 g in an open, shallow 100-mL porcelain dish until it ignites, and allow it to burn without further application of heat in a place free from drafts. Cool, moisten the residue with 0.5 mL of sulfuric acid, and ignite to constant weight: the weight of the residue does not exceed 5 mg (0.01%).

ORGANIC IMPURITIES

• **PROCEDURE 1: RELATED COMPOUNDS**

System suitability solution: 0.5 mg/mL each of USP Diethylene Glycol RS and USP Glycerin RS

Sample solution: 50 mg/mL of Glycerin

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 30-m fused-silica analytical column coated with 3.0-µm G43 stationary phase, and an inlet liner having an inverted cup or spiral structure

Temperature

Injector: 220°

Detector: 250°

Column: See the temperature program table below.

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
100	—	100	—
100	7.5	220	4

Carrier gas: Helium

Injection size: 0.5 µL

Linear velocity: 38 cm/s

Injection type: Split ratio, about 10:1

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 7.0 between diethylene glycol and glycerin

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity, excluding any solvent peaks and diethylene glycol, in the portion of Glycerin taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*

r_T = sum of the responses of all the peaks from the *Sample solution*

Acceptance criteria

Individual impurities: NMT 0.1%

Total impurities: NMT 1.0%

• **Procedure 2: Limit of Chlorinated Compounds**

Sample: 5 g of Glycerin

Analysis: Transfer the *Sample* into a dry, round-bottom, 100-mL flask. Add 15 mL of morpholine, and connect the flask by a ground joint to a reflux condenser. Reflux gently for 3 h. Rinse the condenser with 10 mL of water, receiving the washings in the flask, and cautiously acidify with nitric acid. Transfer the solution to a suitable comparison tube, add 0.50 mL of silver nitrate TS, and dilute with water to 50.0 mL.

Acceptance criteria: The turbidity is not greater than that of a blank to which 0.20 mL of 0.020 N hydrochloric acid has been added, the refluxing being omitted (NMT 30 ppm of Cl).

• **Procedure 3: Fatty Acids and Esters**

Sample solution: Mix 50 g of Glycerin with 50 mL of freshly boiled water and 5 mL of 0.5 N sodium hydroxide VS. Boil the mixture for 5 min, cool, and add phenolphthalein TS.

Analysis: Titrate the excess alkali with 0.5 N hydrochloric acid VS. Perform a blank determination (see ▲*Titrimetry ⟨541⟩*▲ (CN 1-Aug-2024)).

Acceptance criteria: NMT 1 mL of 0.5 N sodium hydroxide is consumed.

SPECIFIC TESTS

• **Color:** When viewed downward against a white surface in a 50-mL color-comparison tube, the color is not darker than the color of a standard made by diluting 0.40 mL of ferric chloride CS with water to 50 mL and similarly viewed in a color-comparison tube of approximately the same diameter and color as that containing the Glycerin.

• **Specific Gravity ⟨841⟩:** NLT 1.249

• **Water Determination, *Method I*⟨921⟩:** NMT 5.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **USP Reference Standards ⟨11⟩**

USP Diethylene Glycol RS

USP Ethylene Glycol RS

USP Glycerin RS

1,2,3-Propanetriol.

$C_3H_8O_3$ 92.10

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

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

Chromatographic Database Information: Chromatographic Database

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