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Diethylene Glycol Monoethyl Ether

$C_6H_{14}O_3$ 134.17

DEFINITION

Diethylene Glycol Monoethyl Ether contains NLT 99.0% and NMT 101.0% of $C_6H_{14}O_3$. It is produced by condensation of ethylene oxide and alcohol, followed by distillation.

IDENTIFICATION

Change to read:

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

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *System suitability solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Sample: Diethylene Glycol Monoethyl Ether (neat)

System suitability solution: 1 mg/mL each of 2- methoxyethanol, 2-ethoxyethanol, ethylene glycol, diethylene glycol, and USP Diethylene Glycol Monoethyl Ether RS in methanol

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 30-m fused-silica bonded with a 1.0-µm layer of phase G46

Temperature

Injector: 250°

Detector: 275°

Column: See the temperature program table below.

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
120	—	120	1
120	12	225	2

Carrier gas: Helium

Flow rate: 2.2 mL/min

Injection size: 0.5 µL

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for 2-methoxyethanol, 2-ethoxyethanol, ethylene glycol, diethylene glycol monoethyl ether, and diethylene glycol are about 0.40, 0.43, 0.50, 0.93, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between 2-ethoxyethanol and ethylene glycol

Relative standard deviation: NMT 2.0%, determined from diethylene glycol monoethyl ether

Analysis

Sample: Diethylene Glycol Monoethyl Ether (neat)

Calculate the percentage of diethylene glycol monoethyl ether ($C_6H_{14}O_3$) in the portion of Diethylene Glycol Monoethyl Ether taken:

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

r_U = peak response for diethylene glycol monoethyl ether

r_T = sum of the responses of all the peaks

Acceptance criteria: 99.0%–101.0%

IMPURITIES

Organic Impurities

- **Procedure 1: Limit of Free Ethylene Oxide**

Acetaldehyde solution: 10 µg/mL of acetaldehyde. [Note—Prepare fresh just before use.]

Ethylene oxide stock solution

[**Caution—**Ethylene oxide is toxic and flammable. Prepare these solutions in a well-ventilated fume hood, using great care. Protect both hands and face by wearing polyethylene protective gloves and an appropriate face mask.]

[Note—Before using the polyethylene glycol 200 in this test, remove any volatile components from it by placing 500 mL of the polyethylene glycol 200 in a 1000-mL round-bottom flask, attaching the flask to a rotary evaporator, and evaporating at a temperature of 60° at a pressure of 1.5–2.5 kPa for 6 h.]

Fill a chilled pressure bottle with liquid ethylene oxide, and store in a freezer when not in use. Use a small piece of polyethylene film to protect the liquid from contact with the rubber gasket. Tare a glass-stoppered conical flask, add 50 mL of polyethylene glycol 200, and reweigh the flask. Transfer 5 mL of the liquid ethylene oxide to a 100-mL beaker chilled in a mixture of sodium chloride and wet ice (1:3). Using a gas-tight gas chromatographic syringe that has been previously cooled to −10°, transfer 300 µL (corresponding to about 250 mg) of liquid ethylene oxide to the polyethylene glycol 200, and swirl gently to mix. Replace the stopper, reweigh the flask, and determine the amount of ethylene oxide absorbed by weight difference. Adjust the weight of the mixture with polyethylene glycol 200 to 100.0 g, replace the stopper, and swirl gently to mix. This stock solution contains 2.5 mg/g of ethylene oxide. [Note—Prepare this *Ethylene oxide stock solution* fresh just before use, and store in a refrigerator.]

Ethylene oxide standard solution A: Tare a glass-stoppered conical flask, and chill it in a refrigerator. Add 35 mL of polyethylene glycol 200, and reweigh the flask. Use a gas-tight gas chromatographic syringe that has been chilled in a refrigerator, and transfer 1 g of the chilled *Ethylene oxide stock solution* to the tared, conical flask. Adjust the weight of the solution with polyethylene glycol 200 to 50.0 g, replace the stopper, and swirl gently to mix. Transfer 10 g of this solution to a 50-mL volumetric flask. Add 30 mL of water, and mix. Dilute with water to volume, and mix to obtain a solution containing 10 µg/mL of ethylene oxide. [Note—Prepare this solution fresh just before use, and store in a refrigerator.]

Ethylene oxide standard solution B: Transfer 10.0 mL of *Ethylene oxide standard solution A* to a 50-mL volumetric flask, and dilute with water to volume to obtain a solution containing 2 µg/mL of ethylene oxide. [Note—Prepare this solution fresh just before use, and store in a refrigerator.]

System suitability solution: Transfer 0.5 mL of *Ethylene oxide standard solution B* to a 10-mL pressure headspace vial, and add 0.1 mL of *Acetaldehyde solution* and 0.1 mL of water, seal the vial, and mix. Heat the mixture at 70° for 45 min.

Standard solution: Transfer 1 g of Diethylene Glycol Monoethyl Ether to a 10-mL pressure headspace vial, and add 0.5 mL of *Ethylene oxide standard solution B* and 0.5 mL of water. Seal the vial, and mix. Heat the mixture at 70° for 45 min.

Sample solution: Transfer 1 g of Diethylene Glycol Monoethyl Ether to a 10-mL pressure headspace vial, add 1 mL of water, seal the vial, and mix. Heat the mixture at 70° for 45 min.

Chromatographic system

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

[Note—The use of a headspace apparatus that automatically transfers a measured amount of headspace is allowed.]

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 30-m glass or quartz capillary bonded with a 1.0-µm layer of phase G1

Temperature

Injector: 150°

Detector: 250°

Column: See the temperature program table below.

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	—	50	5
50	5	180	—

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
180	30	230	5

Carrier gas: Helium

Flow rate: 1 mL/min

Injection size: 1 mL

System suitability

Sample: Gaseous headspace of the *System suitability solution*

[NOTE—The relative retention times for acetaldehyde and ethylene oxide are about 0.94 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between the acetaldehyde and ethylene oxide peaks

Relative standard deviation: NMT 15%

Analysis

Samples: Gaseous headspace of the *Standard solution* and *Sample solution*

[NOTE—Use a heated, gas-tight gas chromatographic syringe.]

Calculate the amount of ethylene oxide in the portion of Diethylene Glycol Monoethyl Ether taken:

$$\text{Result} = r_U/[(r_S \times W_U) - (r_U \times W_S)]$$

r_U = ethylene oxide peak area from the *Sample solution*

r_S = ethylene oxide peak area from the *Standard solution*

W_U = weight of Diethylene Glycol Monoethyl Ether taken to prepare the *Sample solution* (g)

W_S = weight of Diethylene Glycol Monoethyl Ether taken to prepare the *Standard solution* (g)

Acceptance criteria: NMT 1 µg/g

- **PROCEDURE 2: LIMIT OF 2-METHOXYETHANOL, 2-ETHOXYETHANOL, ETHYLENE GLYCOL, AND DIETHYLENE GLYCOL**

Sample, System suitability solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis: Proceed as directed in the *Assay*.

Calculate the percentage of 2-methoxyethanol in the portion of Diethylene Glycol Monoethyl Ether taken:

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

r_U = peak response for 2-methoxyethanol

r_T = sum of all the peak responses

Calculate the percentage of 2-ethoxyethanol in the portion of Diethylene Glycol Monoethyl Ether taken:

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

r_U = peak response for 2-ethoxyethanol

r_T = sum of all the peak responses

Calculate the percentage of ethylene glycol in the portion of Diethylene Glycol Monoethyl Ether taken:

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

r_U = peak response for ethylene glycol

r_T = sum of all the peak responses

Calculate the percentage of diethylene glycol in the portion of Diethylene Glycol Monoethyl Ether taken:

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

r_U = peak response for diethylene glycol

r_T = sum of all the peak responses

Acceptance criteria: See *Impurity Table 1*.

Impurity Table 1

Name	Acceptance Criteria, NMT (ppm)
2-Methoxyethanol	50
2-Ethoxyethanol	160
Ethylene glycol	620
Diethylene glycol	150

SPECIFIC TESTS

• **Refractive Index ⟨831⟩:** 1.426–1.428 at 20°

• **Water Determination, *Method I* ⟨921⟩:** NMT 0.1%, determined on a 10-g specimen

• **Fats and Fixed Oils, *Acid Value*⟨401⟩**

[Note—This test must be performed promptly after sampling to avoid oxidation of the sample specimen.]

Analysis: Dissolve 30 g of Diethylene Glycol Monoethyl Ether in 30 mL of neutralized alcohol. Add 1 mL of phenolphthalein TS, and titrate with 0.01 N alcoholic potassium hydroxide VS to produce a permanent, faint pink color.

Acceptance criteria: The acid value so obtained is NMT 0.1.

• **Fats and Fixed Oils, *Peroxide Value* ⟨401⟩:** NMT 8.0, 2 g being used

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers under an atmosphere of an inert gas, at a temperature not exceeding 35°.

• **Labeling:** Label it to indicate that it is intended for topical or transdermal use only and it is stored under an atmosphere of an inert gas. The material is not to be used for parenterals.

• **USP Reference Standards ⟨11⟩**

USP Diethylene Glycol Monoethyl Ether RS

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

Topic/Question	Contact	Expert Committee
DIETHYLENE GLYCOL MONOETHYL ETHER	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

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