Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: NF Monographs
DocId: GUID-371BF6ED-9DC3-42E9-959A-49063CB178A4_2_en-US
DOI: https://doi.org/10.31003/USPNF_M3751_02_01
DOI Ref: 0b9ks

Propanediol

$C_3H_8O_2$ 76.09

1,3-Propanediol;
1,3-Dihydroxypropane;
Propane, 1-3-diol;
Trimethylene glycol CAS RN®: 504-63-2.

DEFINITION

Propanediol contains NLT 99.7% of 1,3-propanediol ($C_3H_8O_2$). It may be of vegetable, other natural source, or synthetic origin.

IDENTIFICATION

Change to read:

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

• **B.** The retention time of the major peak of the *Sample solution* corresponds to the 1,3-propanediol peak of the *System suitability solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

System suitability solution: Mix quantities of USP Propylene Glycol RS and USP 1,3-Propanediol RS to obtain a solution containing about 5% propylene glycol and 95% propanediol.

Sample solution: Propanediol (neat)

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.25-mm × 30-m capillary column; bonded with a 0.25-µm layer of phase G16

Temperatures

Detector: 250°

Injection port: 250°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	15	200	—
200	40	250	17

Carrier gas: Helium

Flow rate: 1.1 mL/min

Injection volume: 0.2 µL

Split type: Split ratio of 18:1

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for propylene glycol and propanediol are 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between the peaks due to propylene glycol and propanediol

Analysis

Sample: *Sample solution*

Calculate the percentage of propanediol in the portion of sample taken:

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

r_U = peak response for propanediol in the *Sample solution*

r_T = sum of all peak responses in the *Sample solution*

Acceptance criteria: NLT 99.7%

IMPURITIES

• **LIMIT OF RELATED GLYCOL SUBSTANCES**

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

Analysis

Sample: *Sample solution*

Calculate the percentage of each individual impurity in the portion of Propanediol taken:

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

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

r_T = sum of all peak responses in the *Sample solution*

Acceptance criteria

Each individual impurity: NMT 0.1%

Total impurities: NMT 0.3%

• **LIMIT OF ALDEHYDES**

Formaldehyde methanol solution:[1] A solution containing 37% (w/w) of formaldehyde and 10%–15% (w/w) of methanol in water

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

Quantification of Formaldehyde methanol solution: To 2.0 g of *Formaldehyde methanol solution*, add 100 mL of a freshly prepared 100 mg/mL solution of sodium sulfite in carbon-dioxide free water. Add 0.1 mL of *Phenolphthalein solution*, and titrate with 0.5 N sulfuric acid until the color changes from pink to colorless. Carry out a blank titration.

Calculate the percentage content of formaldehyde in *Formaldehyde methanol solution* using the following expression:

$$\text{Result } (P_{HCHO}) = \{[(V_S - V_B) \times N \times M_W \times F]/W\} \times 100$$

V_S = volume of 0.5 N sulfuric acid used in the assay (mL)

V_B = volume of 0.5 N sulfuric acid used in the blank (mL)

N = normality of the titrant (mEq/mL)

M_W = milliequivalent weight of formaldehyde, 30.03 mg/mEq

F = unit conversion factor, 10^{-3} g/mg

W = weight of sample (g)

Standard stock solution: 1.2 µg/mL of *Formaldehyde methanol solution* in carbon-dioxide free water, prepared from appropriately diluting *Formaldehyde methanol solution* in carbon-dioxide free water

Standard solutions: Introduce into 50-mL volumetric flasks 1.0-, 3.0-, 5.0-, 10.0-, 15.0-, and 25.0-mL of *Standard stock solution*, respectively. Calculate the content of formaldehyde, in µg, in the *Standard solutions* using the following expression. Proceed as directed in the *Analysis* below.

$$\text{Result (content of formaldehyde)} = V \times C \times P_{HCHO} \times 0.01$$

V = volume of the *Standard stock solution* added into the *Standard solution* (mL)

C = concentration of *Formaldehyde methanol solution* in the *Standard stock solution* (µg/mL)

P_{HCHO} = percentage content of formaldehyde in *Formaldehyde methanol solution*, as determined above

Sample solution: Introduce 5.0 mL of 0.2 g/mL of propanediol in carbon-dioxide free water into a 50-mL volumetric flask. Proceed as directed in the *Analysis* below.

Blank solution: Prepare in the same manner as for the *Standard solutions* but omitting the *Standard stock solution*.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: Vis spectrophotometry

Analytical wavelength: 655 nm

Analysis

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

To each flask of the *Blank solution*, *Standard solutions*, and *Sample solution* add 2 mL of a freshly prepared 5 mg/mL solution of methylbenzothiazolone hydrazone hydrochloride adjusted with 0.02 N sodium hydroxide to a pH of 4.0. Allow the solutions to stand for 30 min. Add 5 mL of a freshly prepared 7 mg/mL solution of ferric chloride. Cap and swirl the flasks. Allow to stand for 5 min. Add methanol to each flask, and dilute with methanol to 50.0 mL. Mix thoroughly, then allow to stand for 1 min.

Measure the absorbance of the solutions using the treated *Blank solution* as compensation liquid.

Plot the absorbance of the treated *Standard solution* versus the content of formaldehyde, in µg, in the *Standard solution*. Obtain the content of formaldehyde W_{HCHO}, in µg, in the treated *Sample solution* based on the calibration curve.

Calculate the content of aldehydes expressed as formaldehyde (HCHO) in the portion of Propanediol taken:

$$\text{Result} = W_{HCHO}/(C \times V)$$

W_{HCHO} = content of formaldehyde in the treated *Sample solution*, determined from the calibration curve (µg)

C = concentration of Propanediol in the *Sample solution* (g/mL)

V = volume of the *Sample solution* in the analysis (mL)

Acceptance criteria: NMT 20 µg/g, expressed as HCHO.

SPECIFIC TESTS

• **Acidity**

Sample: 50 mL of Propanediol

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

Titrimetric system

(See *Titrimetry ⟨541⟩*)

Mode: Direct titration

Titrant: 0.01 N sodium hydroxide VS

Endpoint detection: Visual

Analysis: To 50 mL of water, add 1 mL of *Phenolphthalein solution*, then add *Titrant* until the solution remains pink for 30 s. Add the *Sample*, and titrate with *Titrant* until the color turns back to pink and remains for more than 30 s.

Calculate the acidity, as acetic acid (CH_3COOH):

$$\text{Result} = (V_T \times N \times W_{Meq})/V_S$$

V_T = *Titrant* volume (mL)

N = *Titrant* normality (mEq/mL)

W_{MEq} = milliequivalent weight of acetic acid, 60.05 mg/mEq

V_S = volume of Propanediol in the *Sample* (mL)

Acceptance criteria: NMT 0.1 mg/mL, calculated as acetic acid (CH_3COOH)

• **Water Determination, *Method Ic* ⟨921⟩:** NMT 0.1%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Do not store above 50°. Protect from moisture.

• **Labeling:** Label it to indicate whether Propanediol is derived from vegetable, other natural source, or synthetic origin.

• **USP Reference Standards ⟨11⟩**
USP 1,3-Propanediol RS
USP Propylene Glycol RS

[1] Formaldehyde TS can be used for *Formaldehyde methanol solution*.

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

Topic/Question	Contact	Expert Committee
PROPANEDIOL	Documentary Standards Support	SE2020 Simple Excipients
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 38(2)

Current DocID: GUID-371BF6ED-9DC3-42E9-959A-49063CB178A4_2_en-US
DOI: https://doi.org/10.31003/USPNF_M3751_02_01
DOI ref: 0b9ks