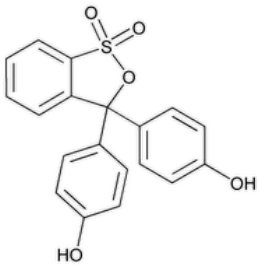
Status: Currently Official on 16-Feb-2025
Official Date: Official Prior to 2013
Document Type: NF Monographs
DocId: GUID-FB1EB875-3573-408D-83A2-77F85E437A42_2_en-US
DOI: https://doi.org/10.31003/USPNF_M461_02_01
DOI Ref: ub8de

Phenolsulfonphthalein



$C_{19}H_{14}O_5S$ 354.38

Phenol red;

Phenol, 4,4'-(3*H*-2,1-benzoxathiol-3-ylidene)bis-,(*S*,*S*-dioxide);

3,3-Bis(4-hydroxyphenyl)-3*H*-2,1-benzoxathiole 1,1-dioxide CAS RN®: 143-74-8.

DEFINITION

Phenolsulfonphthalein contains NLT 98.0% and NMT 102.0% of 4,4'-(3*H*-2,1-benzoxathiol-3-ylidene)bis-,(*S*,*S*-dioxide) phenol ($C_{19}H_{14}O_5S$), calculated on the dried basis.

IDENTIFICATION

- **A.**

Sample: 5 mg of Phenolsulfonphthalein

Analysis: Transfer the *Sample* to a 100-mL volumetric flask, dissolve in and dilute with sodium carbonate solution (1 in 100) to volume, and mix. Dilute 5.0 mL of the solution so obtained to 100.0 mL with sodium carbonate solution (1 in 100). Examine between 400 and 630 nm.

Acceptance criteria: The solution exhibits an absorption maximum at 558 nm, and the specific absorbance at the maximum is between 1900 and 2100.

- **B.**

Sample: 10 mg of Phenolsulfonphthalein

Analysis: Dissolve the *Sample* in 2 mL of 1 N sodium hydroxide, and add 8 mL of water. To 5 mL of the solution so obtained add 1 mL of 0.1 N potassium bromide–bromate and 1 mL of diluted hydrochloric acid, shake, and allow to stand for 15 min. Render the solution alkaline with 1 N sodium hydroxide.

Acceptance criteria: An intense violet-blue color is produced.

ASSAY

- **Procedure**

Sample: 0.9 g

Titrimetric system

(See *Titrimetry* ⟨541⟩.)

Mode: Residual titration

Titrant: 0.1 N sodium thiosulfate VS

Endpoint detection: Visual

Analysis: Transfer the *Sample* to a 250-mL volumetric flask, dissolve in 15 mL of 1 N sodium hydroxide, dilute with water to volume, and mix. Transfer 10.0 mL of the solution so obtained to a glass-stoppered flask. Add 25 mL of glacial acetic acid, 20.0 mL of 0.1 N potassium bromate VS, 5 mL of potassium bromide solution (1 in 10), and 5 mL of hydrochloric acid, and immediately insert the stopper into the flask. Allow to stand protected from light for 15 min. Quickly add 10 mL of potassium iodide solution (1 in 10), taking care to avoid the escape of bromine vapor. Immediately insert the stopper into the flask, and shake vigorously. Rinse the stopper and the neck of the flask with a small

quantity of water. Titrate the liberated iodine with 0.1 N sodium thiosulfate VS, using starch TS as the indicator. Perform a blank determination, and note the difference in volumes required. Each mL of the difference in volumes of 0.1 N sodium thiosulfate is equivalent to 4.43 mg of phenolsulfonphthalein ($C_{19}H_{14}O_5S$).

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩**

Sample: 0.5 g

Acceptance criteria: NMT 0.2%

• **Chromatographic Purity**

Sample solution A: 20 mg/mL of Phenolsulfonphthalein in 0.1 N sodium hydroxide

Sample solution B: Transfer 0.5 mL of *Sample solution A* to a 100-mL volumetric flask, dilute with 0.1 N sodium hydroxide to volume, and mix.

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: *tert*-Amyl alcohol, glacial acetic acid, and water (4:1:1)

Analysis

Samples: *Sample solution A* and *Sample solution B*

Allow the plate to air-dry until the solvent has evaporated, and expose the plate to ammonia vapor. Examine the plate under short-wavelength UV light.

Acceptance criteria: NMT 0.5%; NMT one spot, apart from the principal spot, appears in the chromatogram from *Sample solution A*. This spot is not more intense than the spot in the chromatogram from *Sample solution B*.

• **Insoluble Substances**

Sample: 1 g of finely powdered Phenolsulfonphthalein

Analysis: To the *Sample* add a solution of 0.5 g of sodium bicarbonate in 12 mL of water. Allow to stand for 1 h, shaking frequently. Dilute with sufficient water to make 100 mL, and allow to stand for 15 h. Centrifuge at 2000–3000 *g* for 30 min, and decant the supernatant. Wash the residue first with 25 mL of sodium bicarbonate solution (1 in 100), then with 25 mL of water, and dry at 105°.

Acceptance criteria: The weight of the insoluble residue does not exceed 0.5% of the weight of the Phenolsulfonphthalein taken.

SPECIFIC TESTS

• **Visual Transition Interval**

Potassium chloride solution: Dissolve 1.0 g of potassium chloride in 100 mL of water, and adjust with 0.01 N hydrochloric acid or sodium hydroxide to a pH of 6.8.

Sample solution: Dissolve 0.1 g of Phenolsulfonphthalein in 100 mL of alcohol.

Analysis 1: Add 0.15 mL of the *Sample solution* to the *Potassium chloride solution*.

Acceptance criteria 1: The color is yellow with NMT a faint trace of green color.

Analysis 2: Titrate the solution from *Analysis 1* with 0.01 N sodium hydroxide to a pH of 7.0.

Acceptance criteria 2: The color of the solution becomes orange.

Analysis 3: Continue the titration of the solution from *Analysis 2* with 0.01 N sodium hydroxide to a pH of 8.2.

Acceptance criteria 3: The color of the solution becomes red. NMT 0.20 mL of 0.01 N sodium hydroxide is consumed in the entire titration.

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 10^3 cfu/g, and the total combined molds and yeasts count does not exceed 10^2 cfu/g.

• **Loss on Drying ⟨731⟩**

Sample: 1 g of powdered Phenolsulfonphthalein

Analysis: Dry the *Sample* at 105° to constant weight.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. No storage requirements specified.

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

Topic/Question	Contact	Expert Committee
PHENOLSULFONPHTHALEIN	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 31(1)

Current DocID: GUID-FB1EB875-3573-408D-83A2-77F85E437A42_2_en-US
Previous DocID: GUID-FB1EB875-3573-408D-83A2-77F85E437A42_1_en-US
DOI: https://doi.org/10.31003/USPNF_M461_02_01
DOI ref: ub8de