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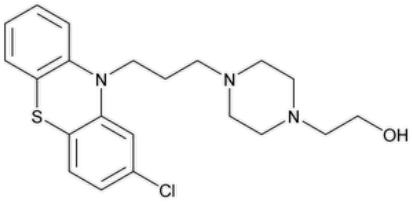
Perphenazine



$C_{21}H_{26}ClN_3OS$ 403.97

Piperazineethanol, 4-[3-(2-chloro-10*H*-phenothiazin-10-yl)propyl-];

4-[3-(2-Chlorophenothiazin-10-yl)propyl]-1-piperazineethanol CAS RN®: 58-39-9; UNII: FTA7XXY4EZ.

DEFINITION

Perphenazine contains NLT 98.0% and NMT 102.0% of perphenazine ($C_{21}H_{26}ClN_3OS$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

• **B.** The retention time of the major peak of the *Diluted sample solution* corresponds to that of the *Standard solution*, as obtained in the test for *Organic Impurities*.

ASSAY

• **Procedure**

Sample solution: Dissolve 0.150 g of Perphenazine in 25 mL of glacial acetic acid.

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Direct titration

Titrant: 0.1 N perchloric acid VS

Endpoint detection: Potentiometric

Analysis

Sample: *Sample solution*

Titrate the *Sample solution* with *Titrant*. Carry out a blank titration.

Calculate the percentage of perphenazine ($C_{21}H_{26}ClN_3OS$) in the portion of Perphenazine taken:

$$\text{Result} = [(V - B) \times N \times F/W] \times 100$$

V = *Titrant* volume consumed by the *Sample* (mL)

B = *Titrant* volume consumed by the blank (mL)

N = normality of the *Titrant* (meq/mL)

F = equivalent weight of perphenazine, 202.0 mg/meq

W = *Sample* weight (mg)

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Organic Impurities**

Prepare the solutions immediately before use. Carry out the test protected from light.

Solution A: Acetonitrile and 7 g/L of monobasic sodium phosphate dihydrate in water (35:65)

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
5	100	0
10	80	20
33	30	70
48	100	0

System suitability solution: 2 mg/mL of USP Perphenazine RS, 0.002 mg/mL of USP Perphenazine Sulfoxide RS, and 0.002 mg/mL of USP Perphenazine Related Compound B RS in *Solution A*

Standard solution: 0.002 mg/mL of USP Perphenazine RS in *Solution A*

Sample solution: 2 mg/mL of Perphenazine in *Solution A*

Diluted sample solution: 0.002 mg/mL of Perphenazine in *Solution A* from the *Sample solution*

Chromatographic system

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

Mode: LC

Detector: UV 245 nm

Column: 4.0-mm × 25-cm; 4-µm packing L7

Column temperature: 30°

Flow rate: 1.3 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 3.0 between perphenazine and perphenazine related compound B, *System suitability solution*

Tailing factor: NMT 2.5, *Standard solution*

Relative standard deviation: NMT 10.0%, *Standard solution*

Analysis

Samples: *Standard solution, Sample solution*, and *Diluted sample solution*. [Note—*Diluted sample solution* is used for *Identification* test *B*.]

Calculate the percentage of impurities in the portion of Perphenazine taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response for each impurity from the *Sample solution*

r_S = peak response of perphenazine from the *Standard solution*

C_S = concentration of USP Perphenazine RS in the *Standard solution* (mg/mL)

C_U = concentration of Perphenazine in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Perphenazine sulfoxide	0.3	1.6	0.2
Perphenazine related compound B	0.8	1.0	0.5
Perphenazine	1.0	—	—
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry a sample in a vacuum at 65° for 4 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

• **USP Reference Standards** ⟨11⟩

USP Perphenazine RS

USP Perphenazine Related Compound B RS

2-{4-[3-(10*H*-Phenothiazin-10-yl)propyl]piperazin-1-yl}ethanol.

$C_{21}H_{27}N_3OS$ 369.52

USP Perphenazine Sulfoxide RS

2-Chloro-10-{3-[4-(2-hydroxyethyl)piperazin-1-yl]propyl}-10*H*-phenothiazine 5-oxide.

$C_{21}H_{26}ClN_3O_2S$ 419.97

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

Topic/Question	Contact	Expert Committee
PERPHENAZINE	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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