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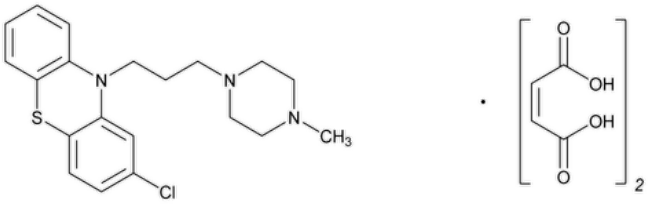
Prochlorperazine Maleate



$C_{20}H_{24}ClN_3S \cdot 2C_4H_4O_4$ 606.09

10*H*-Phenothiazine, 2-chloro-10-[3-(4-methyl-1-piperazinyl)propyl]-, (*Z*)-2-butenedioate (1:2);

2-Chloro-10-[3-(4-methylpiperazin-1-yl)propyl]phenothiazine maleate (1:2) CAS RN®: 84-02-6; UNII: I1T8O1JTL6.

DEFINITION

Prochlorperazine Maleate contains NLT 98.0% and NMT 102.0% of prochlorperazine maleate ($C_{20}H_{24}ClN_3S \cdot 2C_4H_4O_4$), calculated on the dried basis.

[NOTE—Throughout the following procedures, protect the samples, the Reference Standard, and solutions containing them from light, and conduct the procedures without delay.]

IDENTIFICATION

Change to read:

• **A.** ▲**SPECTROSCOPIC IDENTIFICATION TESTS ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K.▲ (CN 1-May-2020)

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

ASSAY

• **PROCEDURE**

Ion-pairing solution: Dissolve 4.33 g of sodium 1-octanesulfonate in 500 mL of water. Add 4.0 mL of glacial acetic acid, and dilute with water to 1 L.

Mobile phase: Acetonitrile, methanol, and *Ion-pairing solution* (40:15:45)

Standard solution: 0.2 mg/mL of USP Prochlorperazine Maleate RS in *Mobile phase*. Sonicate to dissolve, if needed, prior to final dilution.

Sample solution: 0.2 mg/mL of Prochlorperazine Maleate in *Mobile phase*. Sonicate to dissolve, if needed, prior to final dilution.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1 or 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of prochlorperazine maleate ($C_{20}H_{24}ClN_3S \cdot 2C_4H_4O_4$) in the portion of Prochlorperazine Maleate taken:

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

r_U = peak response of prochlorperazine from the *Sample solution*

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

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

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

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Buffer: 1.36 g/L of sodium acetate trihydrate in water (0.01 M). Add 2.0 mL of triethylamine and 6.0 mL of glacial acetic acid per L of solution.

Solution A: *Buffer*

Solution B: Acetonitrile

Mobile phase: See *Table 1*. Return to original conditions, and re-equilibrate the system for about 10 min.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	75	25
20	65	35
25	65	35
55	35	65
65	35	65

Diluent: Acetonitrile and water (40:60)

Impurity stock solution: 0.16 mg/mL of USP Prochlorperazine Related Compound A RS in *Diluent*

Standard stock solution: 0.16 mg/mL of USP Prochlorperazine Maleate RS in *Diluent*

System suitability solution: 1.6 µg/mL each of USP Prochlorperazine Maleate RS and USP Prochlorperazine Related Compound A RS in *Diluent* from the *Standard stock solution* and the *Impurity stock solution*, respectively

Standard solution: 6.4 µg/mL of USP Prochlorperazine Maleate RS in *Diluent* from the *Standard stock solution*

Sensitivity solution: 0.32 µg/mL of USP Prochlorperazine Maleate RS in *Diluent* from the *Standard solution*

Sample solution: 0.64 mg/mL of Prochlorperazine Maleate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 50 ± 5°

Flow rate: 2.0 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between prochlorperazine related compound A and prochlorperazine, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Prochlorperazine Maleate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times (1/F) \times 100$$

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

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

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

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

M_{r1} = molecular weight of prochlorperazine, 373.94

M_{r2} = molecular weight of prochlorperazine maleate, 606.09

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

Acceptance criteria: See *Table 2*. Disregard any peak below 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor[a]	Acceptance Criteria, NMT (%)
Maleic acid	0.07	—	Disregard
Prochlorperazine sulfoxide[b]	0.20	0.38	0.15
Perazine[c]	0.66	1.0	0.15
Prochlorperazine 4-chloro isomer (prochlorperazine related compound A)[d]	0.97	0.61	0.15
Prochlorperazine	1.00	—	—
4-Chlorophenothiazine[e]	2.01	1.9	0.1
2-Chlorophenothiazine[f]	2.08	2.1	0.1
Specified unknown 1	2.64	1.0	0.50
Specified unknown 2	2.79	1.0	0.50
Specified unknown 3	2.88	1.0	0.20
Any other individual impurity	—	1.0	0.10
Total impurities	—	—	1.5

[a] *F* values are based on the response of prochlorperazine (free base).

[b] 2-Chloro-10-[3-(4-methylpiperazin-1-yl)propyl]-10*H*-phenothiazine sulfoxide.

[c] 10-[3-(4-Methylpiperazin-1-yl)propyl]-10*H*-phenothiazine.

[d] 4-Chloro-10-[3-(4-methylpiperazin-1-yl)propyl]-10*H*-phenothiazine.

[e] 4-Chloro-10*H*-phenothiazine.

[f] 2-Chloro-10*H*-phenothiazine.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry under vacuum at 60° for 2 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at room temperature.

• **USP Reference Standards** ⟨11⟩

USP Prochlorperazine Maleate RS

USP Prochlorperazine Related Compound A RS

4-Chloro-10-[3-(4-methylpiperazin-1-yl)propyl]-10*H*-phenothiazine dihydrochloride.

$C_{20}H_{24}ClN_3S \cdot 2HCl$ 443.47

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

Topic/Question	Contact	Expert Committee
PROCHLORPERAZINE MALEATE	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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