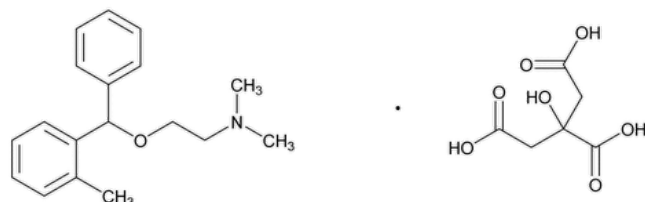


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Orphenadrine Citrate



$C_{18}H_{23}NO \cdot C_6H_8O_7$ 461.50

Ethanamine, *N,N*-dimethyl-2-[(2-methylphenyl)phenylmethoxy]-, ($\pm$)-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1);
 ($\pm$)-*N,N*-Dimethyl-2-[(*o*-methyl- α -phenylbenzyl)oxy]ethylamine citrate (1:1) CAS RN[®]: 4682-36-4; UNII: X0A40N8I4S.

DEFINITION

Orphenadrine Citrate contains NLT 98.0% and NMT 101.5% of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$), 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 *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **C.** [IDENTIFICATION TESTS—GENERAL, Citrate\(191\)](#): Meets the requirements

ASSAY

PROCEDURE

Buffer: 5.8 g/L of monobasic ammonium phosphate in water. Adjust with ammonium hydroxide or phosphoric acid to a pH of 7.9.

Mobile phase: Methanol, acetonitrile, and *Buffer* (45:15:40)

System suitability solution: 0.01 mg/mL each of [USP Orphenadrine Related Compound B RS](#), [USP Orphenadrine Related Compound C RS](#), and [USP Methylbenzhydrol RS](#) and 1.0 mg/mL of [USP Orphenadrine Citrate RS](#) in *Mobile phase*

Standard solution: 1.0 mg/mL of [USP Orphenadrine Citrate RS](#) in *Mobile phase*

Sample solution: 1.0 mg/mL of Orphenadrine Citrate in *Mobile phase*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm; 5- μ m packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 20 μ L

Run time: NLT 2.5 times the retention time of orphenadrine

System suitability

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

[NOTE—See [Table 1](#) for the relative retention times.]

Suitability requirements

Resolution: NLT 3.0 between orphenadrine related compound B and C; NLT 3.0 between orphenadrine related compound C and methylbenzhydrol, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$) in the portion of Orphenadrine Citrate taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Orphenadrine Citrate RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–101.5% on the dried basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

• **ORGANIC IMPURITIES, PROCEDURE 1**

[NOTE—If methyl orphenadrine is a known manufacturing impurity, *Procedure 1* and the test for *Isomer Content* are recommended. If diphenhydramine and didesmethyl orphenadrine are known manufacturing process impurities, *Procedure 2* is recommended.]

Buffer, Mobile phase, System suitability solution, and Chromatographic system: Proceed as directed in the Assay.

Standard solution: 0.001 mg/mL of [USP Orphenadrine Citrate RS](#) in *Mobile phase*

Sensitivity solution: 0.5 µg/mL of [USP Orphenadrine Citrate RS](#), from the *Standard solution*, in *Mobile phase*

Sample solution: 1 mg/mL of Orphenadrine Citrate in *Mobile phase*

System suitability

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

[NOTE—See [Table 1](#) for the relative retention times.]

Suitability requirements

Resolution: NLT 3.0 between orphenadrine related compound B and C; NLT 3.0 between orphenadrine related compound C and 2-methylbenzhydrol, *System suitability solution*

Tailing factor: NMT 2, *Standard 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 impurity in the portion of Orphenadrine Citrate taken:

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

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

r_S = peak area of Orphenadrine Citrate from the *Standard solution*

C_S = concentration of [USP Orphenadrine Citrate RS](#) in the *Standard solution* (mg/mL)

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

F = relative response factor (see [Table 1](#))

Acceptance criteria: See [Table 1](#). Disregard any peak less than 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Citric acid ^a	0.14	—	—