Status: Currently Official on 16-Feb-2025
Official Date: Official Prior to 2013
Document Type: USP Monographs
DocId: GUID-9511255D-32EA-435B-B0DF-DBA2158AC672_2_en-US
DOI: https://doi.org/10.31003/USPNF_M55740_02_01
DOI Ref: 5z6ru

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# Naphazoline Hydrochloride and Pheniramine Maleate Ophthalmic Solution

## DEFINITION

Naphazoline Hydrochloride and Pheniramine Maleate Ophthalmic Solution is a sterile, buffered solution of Naphazoline Hydrochloride and Pheniramine Maleate in water adjusted to a suitable tonicity. It contains NLT 90.0% and NMT 110.0% of the labeled amount of naphazoline hydrochloride ($C_{14}H_{14}N_2 \cdot HCl$) and pheniramine maleate ($C_{16}H_{20}N_2 \cdot C_4H_4O_4$). It contains a suitable preservative.

## IDENTIFICATION

• **A. Thin-Layer Chromatography**

**Standard solution A:** 1.5 mg/mL of USP Naphazoline Hydrochloride RS in water

**Standard solution B:** 6.0 mg/mL of USP Pheniramine Maleate RS in water

**Sample solution:** Equivalent to 0.25 mg/mL of naphazoline hydrochloride and 3 mg/mL of pheniramine maleate in water from Ophthalmic Solution

**Chromatographic system**

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

**Adsorbent:** 0.25-mm layer of silica gel on a 20-cm × 20-cm chromatographic plate

**Application volume:** 5 µL of *Standard solution A*, 10 µL of *Standard solution B*, and 30 µL of the *Sample solution*

**Developing solvent system:** Methanol, acetic acid, and water (8:1:1)

**Spray reagent:** Ninhydrin TS

**Analysis**

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

Allow the spots to dry, then place the plate in a saturated chromatographic chamber, and develop in the *Developing solvent system* until the solvent front has moved to 1.5 cm from the top of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow to air-dry. Spray with *Spray reagent*, and place in an oven at 105° to visualize the spots. Both the naphazoline and pheniramine spots are purplish gray in color.

**Acceptance criteria:** The $R_F$ values of the spots of the *Sample solution* correspond to those of *Standard solution A* and *Standard solution B*.

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

## ASSAY

• **Procedure**

**Buffer solution:** Dissolve 14.2 g of anhydrous dibasic sodium phosphate and 20 mL of triethylamine in 1900 mL of water. Adjust with phosphoric acid to a pH of 5.6 ± 0.1, and dilute with water to 2000 mL.

**Mobile phase:** Acetonitrile and *Buffer solution* (20:80)

**Standard stock solution A:** 0.75 mg/mL of USP Naphazoline Hydrochloride RS in *Mobile phase*

**Standard stock solution B:** 3.00 mg/mL of USP Pheniramine Maleate RS in *Mobile phase*

**Standard solution:** 0.03 mg/mL of naphazoline hydrochloride and 0.36 mg/mL of pheniramine maleate in *Mobile phase* prepared as follows. Transfer 1.0 mL of *Standard stock solution A* and 3.0 mL of *Standard stock solution B* to a 25-mL volumetric flask. Dilute with *Mobile phase* to volume.

**Sample solution:** Transfer a volume of Ophthalmic Solution, equivalent to 0.75 mg of naphazoline hydrochloride and 9.0 mg of pheniramine maleate, to a 25-mL volumetric flask. Dilute with *Mobile phase* to volume.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 270 nm

**Column:** 4.6-mm × 15-cm; packing L7

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**Flow rate:** 1.5 mL/min

**Injection volume:** 25 µL

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

**Resolution:** NLT 2 between the naphazoline and pheniramine peaks

**Column efficiency:** NLT 750 theoretical plates for the naphazoline and pheniramine peaks

**Tailing factor:** NMT 2.5 for pheniramine

**Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of naphazoline hydrochloride ($C_{14}H_{14}N_2 \cdot HCl$) in the portion of Ophthalmic Solution taken:

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

$r_U$ = peak response of naphazoline from the *Sample solution*

$r_S$ = peak response of naphazoline from the *Standard solution*

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

$C_U$ = nominal concentration of naphazoline hydrochloride in the *Sample solution* (mg/mL)

Calculate the percentage of the labeled amount of pheniramine maleate ($C_{16}H_{20}N_2 \cdot C_4H_4O_4$) in the portion of Ophthalmic Solution taken:

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

$r_U$ = peak response of pheniramine from the *Sample solution*

$r_S$ = peak response of pheniramine from the *Standard solution*

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

$C_U$ = nominal concentration of pheniramine maleate in the *Sample solution* (mg/mL)

**Acceptance criteria**

**Naphazoline hydrochloride:** 90.0%–110.0%

**Pheniramine maleate:** 90.0%–110.0%

## SPECIFIC TESTS

- **pH** ⟨791⟩**:** 5.7–6.3
- **Sterility Tests** ⟨71⟩**:** It meets the requirements when tested as directed in *Test for Sterility of the Product to Be Examined, Membrane Filtration*.

## ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, and store at a temperature between 20° and 25°, protected from light.
- **USP Reference Standards** ⟨11⟩

  USP Naphazoline Hydrochloride RS

  USP Pheniramine Maleate RS

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

| Topic/Question | Contact | Expert Committee |
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