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Procaine Hydrochloride and Epinephrine Injection

(*This monograph has been updated to the current USP style. No revisions or changes to tests have been made.*)

DEFINITION

Procaine Hydrochloride and Epinephrine Injection is a sterile solution of Procaine Hydrochloride and Epinephrine Hydrochloride in Water for Injection. The content of epinephrine is NMT 0.002% (1 in 50,000). It contains NLT 95.0% and NMT 105.0% of the labeled amount of procaine hydrochloride ($C_{13}H_{20}N_2O_2 \cdot HCl$), and NLT 90.0% and NMT 115.0% of the labeled amount of epinephrine ($C_9H_{13}NO_3$).

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

  Sample: Evaporate a portion of Injection, equivalent to 20 mg of procaine hydrochloride, on a steam bath just to dryness, and dry over silica gel for 18 h, protected from light. Use the residue for the test.

- **B.**

  Solution A: 100 mg/mL of sodium hydroxide in water

  Solution B: 20 mg/mL of 2-naphthol in *Solution A*

  Analysis: Dissolve 10 mg of the residue obtained in *Identification A* in 1 mL of water, add 1 drop each of hydrochloric acid and 100 mg/mL of sodium nitrite in water, then add 1 mL of *Solution B*, and shake.

  Acceptance criteria: A scarlet-red precipitate is formed.

ASSAY

- **Procaine Hydrochloride**

  Standard solution: Transfer to a 125-mL separator about 50 mg, accurately weighed, of USP Procaine Hydrochloride RS and dissolve in 20 mL of water.

  Sample solution: Transfer to a 125-mL separator an accurately measured volume of Injection, equivalent to about 50 mg of procaine hydrochloride, and dilute with water to 20 mL.

  Instrumental conditions

  Mode: UV

  Analytical wavelength: 280 nm

  Blank: Chloroform

  Analysis

  Samples: *Standard solution* and *Sample solution*

  Add 5 mL of ammonium hydroxide, 6 N, to both the *Standard solution* and *Sample solution*, then treat each as follows. Extract with five 25-mL portions of chloroform, and filter the combined extracts through 1 g of sodium sulfate, anhydrous supported on a pledget of glass wool. Receive the filtrate in a 200-mL volumetric flask, and add chloroform to volume. Transfer 3.0 mL of this solution to a 100-mL volumetric flask, and add chloroform to volume. Concomitantly determine the absorbances of both solutions using the *Blank*.

  Calculate the percentage of the labeled amount of procaine hydrochloride ($C_{13}H_{20}N_2O_2 \cdot HCl$) in the portion of Injection taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

  A_U = absorbance of the *Sample solution*

  A_S = absorbance of the *Standard solution*

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

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

  Acceptance criteria: 95.0%–105.0%

• **Content of Epinephrine**

Solution A: Alcohol, 200 mg/mL of sodium hydroxide in water, and 20 mg/mL of ascorbic acid in water (25:20:2). Prepare fresh on the day of use.

Standard stock solution: 0.18 mg/mL of USP Epinephrine Bitartrate RS prepared as follows. Transfer 18 mg of USP Epinephrine Bitartrate RS in a 100-mL volumetric flask and add sodium bisulfite solution (1 in 1000) to volume.

Standard solution: 10 µg/mL of epinephrine from *Standard stock solution* in water

Sample solution: A portion of Injection nominally equivalent to 10 µg of epinephrine

Instrumental conditions

Mode: Fluorescence

Excitation wavelength: 420 nm

Detection wavelength: 520 nm

Blank: Water

Analysis

Samples: *Standard solution* and *Sample solution*

Pipet 1 mL of the *Sample solution* and *Standard solution* into separate 50-mL beakers. Treat the contents of each beaker as follows. Add 10 mL of dilute hydrochloric acid (1 in 120), and heat gently to reduce the volume of solution to 5 mL. Allow to cool to room temperature, then add 5 mL of sodium acetate solution (1 in 5), followed by 0.5 mL of potassium ferricyanide solution (1 in 400). At 2 min, accurately timed, after the last addition, add 20 mL of *Solution A*, transfer the contents to a corresponding 50-mL volumetric flask with the aid of water, and add water to volume. At 15–20 min after the addition of *Solution A*, determine the fluorescences of each solution and of a reagent blank.

Calculate the percentage of the labeled amount of epinephrine ($C_9H_{13}NO_3$) in the portion of Injection taken:

$$\text{Result} = [(I_U - B)/(I_S - B)] \times (C_S/C_U)$$

I_U = fluorescence reading of the *Sample solution*

B = fluorescence reading of the *Blank*

I_S = fluorescence reading of the *Standard solution*

C_S = concentration of epinephrine of USP Epinephrine Bitartrate RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of epinephrine in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–115.0%

SPECIFIC TESTS

• **Color and Clarity**

Standard solution: 0.1 N iodine VS and water (1:249)

Sample solution: A portion of Injection

Instrumental conditions

Mode: Vis

Analytical wavelength: 460 nm

Cell: 1 cm

Analysis

Samples: *Standard solution* and *Sample solution*

Visually examine a portion of the *Sample solution* in a suitable clear glass test tube against a white background: it is not pinkish and it contains no precipitate. If any yellow color is observed in the *Sample solution*, concomitantly determine the absorbances of the *Sample solution* and the *Standard solution*.

Acceptance criteria: The absorbance of the *Sample solution* does not exceed that of the *Standard solution*.

• **Bacterial Endotoxins Test ⟨85⟩:** It contains NMT 0.6 USP Endotoxin Units/mg of procaine hydrochloride.

• **pH ⟨791⟩:** 3.0–5.5

• **Other Requirements:** Meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose or in multiple-dose, light-resistant containers, preferably of Type I or Type II glass.

• **Labeling:** The label indicates that the Injection is not to be used if its color is pinkish or darker than slightly yellow or if it contains a precipitate.

• **USP Reference Standards ⟨11⟩**

USP Epinephrine Bitartrate RS
USP Procaine Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
PROCAINE HYDROCHLORIDE AND EPINEPHRINE INJECTION	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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