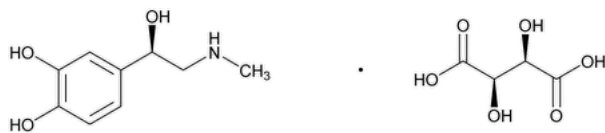


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Epinephrine Bitartrate



$C_9H_{13}NO_3 \cdot C_4H_6O_6$ 333.29

1,2-Benzenediol, 4-[1-hydroxy-2-(methylamino)ethyl]-, (R)-, [R-(R*,R*)]-2,3-dihydroxybutanedioate (1:1) (salt);
 (-)-3,4-Dihydroxy-α-[(methylamino)methyl]benzyl alcohol (+)-tartrate (1:1) salt CAS RN®: 51-42-3.

UNII: 30Q7KI53AK

Change to read:

DEFINITION

Epinephrine Bitartrate contains NLT 97.0% and NMT Δ 103.0% Δ (USP 1-May-2021) of Epinephrine Bitartrate ($C_9H_{13}NO_3 \cdot C_4H_6O_6$), calculated on the dried basis.

IDENTIFICATION

Delete the following:

▲ • PROCEDURE

Sample: 500 mg

Analysis: Dissolve the *Sample* in 20 mL of water containing 100 mg of sodium bisulfite. Add 6 N ammonium hydroxide until the solution has a distinct odor of ammonia, and allow to stand in a refrigerator for 1 h. Filter the precipitate, wash it with three 2-mL portions of cold water, then with 5 mL of cold alcohol, and finally with 5 mL of cold ether, and dry in vacuum over silica gel for 3 h. To 5 mL of pH 4.0 acid phthalate buffer, add 0.5 mL of a slightly acid solution of above obtained Epinephrine (1 in 1000) and 1.0 mL of 0.1 N iodine, and allow to stand for 5 min. Add 2 mL of sodium thiosulfate solution (1 in 40). (See *Reagents, Indicators, and Solutions—Buffer Solutions*.)

Acceptance criteria: A deep red color is produced. Δ (USP 1-May-2021)

Add the following:

▲ • **A.** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#): 197A or 197K Δ (USP 1-May-2021)

Add the following:

▲ • **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*. Δ (USP 1-May-2021)

ASSAY

Change to read:

• PROCEDURE

▲ Protect the *Standard solution* and *Sample solution* from light.

Buffer: 5.0 g/L of [potassium dihydrogen phosphate](#) and 2.6 g/L of [sodium octanesulfonate](#) in [water](#). Adjust with [phosphoric acid](#) to a pH of 2.8. Dilute with [water](#) to volume.

Solution A: [Acetonitrile](#) and *Buffer* (5:95)

Solution B: [Acetonitrile](#) and *Buffer* (45:55)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
20	50	

Time (min)	Solution A (%)	Solution B (%)
21	50	50
23	95	5
30	95	5

Standard solution: 0.91 mg/mL of [USP Epinephrine Bitartrate RS](#) in *Solution A*

Sample solution: 0.91 mg/mL of Epinephrine Bitartrate in *Solution A*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 10-cm; 3-μm packing [L1](#)

Temperatures

Autosampler: 4°

Column: 50°

Flow rate: 1.2 mL/min

Injection volume: 5 μL

Run time: NLT 5.6 times the retention time of epinephrine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.1%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of epinephrine bitartrate ($C_9H_{13}NO_3 \cdot C_4H_6O_6$) in the portion of Epinephrine Bitartrate taken:

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

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

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

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

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

Acceptance criteria: 97.0%–103.0% on the dried basis ▲ (USP 1-May-2021)

IMPURITIES

Change to read:

- [RESIDUE ON IGNITION \(281\)](#): ▲NMT 0.1% ▲ (USP 1-May-2021)

Delete the following:

▲• LIMIT OF ADRENALONE

Sample: 4 mg/mL of Epinephrine Bitartrate in dilute hydrochloric acid (1 in 200)

Instrument conditions

Mode: UV

Analytical Wavelength: 310nm

Cell: 1cm

Analysis: Determine absorptivity.

Acceptance criteria: NMT 0.2 ▲ (USP 1-May-2021)

Delete the following:

▲• LIMIT OF NOREPINEPHRINE BITARTRATE

Standard stock solution A: 200 mg/mL of [USP Epinephrine Bitartrate RS](#) in water

Standard solution A: 20 mg/mL of [USP Epinephrine Bitartrate RS](#) in methanol, from *Standard stock solution A*

Standard stock solution B: 8.0 mg/mL of [USP Norepinephrine Bitartrate RS](#) in water

Standard solution B: 0.80 mg/mL of [USP Norepinephrine Bitartrate RS](#) in methanol, from *Standard stock solution B*

Sample solution: 20 mg/mL of Epinephrine Bitartrate in a mixture of methanol and water (90:10)

