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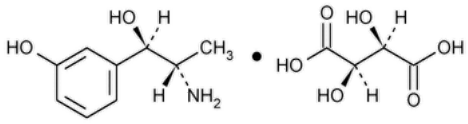
Metaraminol Bitartrate



$C_9H_{13}NO_2 \cdot C_4H_6O_6$ 317.29

Benzenemethanol, α-(1-aminoethyl)-3-hydroxy-, [*R*-(*R**,*S**)]-, [*R*-(*R**,*R**)]-2,3-dihydroxybutanedioate (1:1) (salt);

(−)-α-(1-Aminoethyl)-*m*-hydroxybenzyl alcohol tartrate (1:1) (salt) CAS RN®: 33402-03-8; UNII: ZC4202M9P3.

DEFINITION

Metaraminol Bitartrate contains NLT 98.0% and NMT 102.0% of metaraminol bitartrate ($C_9H_{13}NO_2 \cdot C_4H_6O_6$), calculated on the dried basis.

IDENTIFICATION

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

Solution A: Dissolve 3.24 g of anhydrous octanesulphonic acid sodium salt in 1 L of water.

Solution B: Acetonitrile and water (90:10)

Diluent: Acetonitrile and water (20:80)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
5	80	20
20	5	95
30	5	95
30.1	80	20
40	80	20

Standard solution: 0.75 mg/mL of USP Metaraminol Bitartrate RS in *Diluent*

Sample solution: 0.75 mg/mL of Metaraminol Bitartrate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Column temperature: 35°

Flow rate: 1 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 metaraminol bitartrate ($C_9H_{13}NO_2 \cdot C_4H_6O_6$) in the portion of Metaraminol Bitartrate taken:

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

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

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

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

C_U = concentration of Metaraminol Bitartrate 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**

Solution A, Solution B, Diluent, Mobile phase, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Peak identification solution: 0.1 mg/mL each of USP Metaraminol Bitartrate RS, USP Metaraminol Related Compound A RS, and USP Metaraminol Related Compound B RS in *Diluent*

Sensitivity solution: 0.76 µg/mL of USP Metaraminol Bitartrate RS in *Diluent* from the *Standard solution*

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Tailing factor: NMT 2.0, *Standard solution*

Signal-to-noise ratio: NLT 15, *Sensitivity solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of metaraminol related compound A and any unspecified impurity in the portion of Metaraminol Bitartrate taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of metaraminol related compound A or any unspecified impurity from the *Sample solution*

r_T = sum of all the peak responses from the *Sample solution*

Acceptance criteria: See *Table 2*. Disregard peaks due to tartaric acid and metaraminol related compound B.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Tartaric acid	0.13 and 0.14	—
Metaraminol	1.00	—
Metaraminol related compound B	1.52	—
Metaraminol related compound A	1.82	0.15
Any unspecified impurity	—	0.10
Total impurities	—	1.0

- **Limit of Metaraminol Related Compound B**

Solution A: Dissolve 1.88 g of anhydrous 1-hexane sulfonic acid sodium salt and 1.36 g of monobasic potassium phosphate in 1 L of water. Adjust with dilute phosphoric acid to a pH of 2.6.

Solution B: Acetonitrile and water (85:15)

Diluent: Acetonitrile and water (20:80)

Mobile phase: See *Table 3*.

Table 3

Time (min)	Solution A (%)	Solution B (%)
0	70	30
5	70	30
10	55	45
15	50	50
18	50	50
21	10	90
30	10	90
31	70	30
35	70	30

Standard solution: 0.0012 mg/mL of USP Metaraminol Related Compound B RS in *Diluent*

Sample solution: 0.75 mg/mL of Metaraminol Bitartrate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

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

Column temperature: 35°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 15.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of metaraminol related compound B in the portion of Metaraminol Bitartrate taken:

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

r_U = peak response of metaraminol related compound B from the *Sample solution*

r_S = peak response of metaraminol related compound B from the *Standard solution*

C_S = concentration of USP Metaraminol Related Compound B RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 0.15%

- **Enantiomeric Purity**

Mobile phase: Heptane, methanol, isopropyl alcohol, and methane sulfonic acid (80:10:10:0.2)

Metaraminol enantiomer stock solution: 0.05 mg/mL of USP Metaraminol Enantiomer RS in *Mobile phase*

System suitability solution: 1 mg/mL of USP Metaraminol Bitartrate RS and 0.005 mg/mL of USP Metaraminol Enantiomer RS from *Metaraminol enantiomer stock solution* in *Mobile phase*

Sensitivity solution: 1 µg/mL of USP Metaraminol Bitartrate RS in *Mobile phase*

Sample solution: 1 mg/mL of Metaraminol Bitartrate in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; 3-µm packing L51

Column temperature: 40°

Flow rate: 0.5 mL/min

Injection volume: 10 µL

Run time: NLT 3 times the retention time of metaraminol

System suitability

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

[NOTE—The relative retention times for metaraminol and the metaraminol enantiomer are about 1.0 and 1.1, respectively.]

Suitability requirements

Resolution: NLT 1.5 between the metaraminol and the metaraminol enantiomer peaks, *System suitability solution*

Signal-to-noise ratio: NLT 15, *Sensitivity solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of metaraminol enantiomer in the portion of Metaraminol Bitartrate taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of metaraminol enantiomer from the *Sample solution*

r_T = sum of all the peak responses from the *Sample solution*

Acceptance criteria: NMT 0.15%

SPECIFIC TESTS

Change to read:

• **CONTENT OF TARTARIC ACID**

Sample solution: To 0.1 g of Metaraminol Bitartrate, add 60 mL of dimethylformamide, and sonicate for 2 min.

Titrimetric system

Mode: Direct titration

Titrant: 0.1 N tetrabutylammonium hydroxide VS

Endpoint detection: Potentiometric

Blank: Dimethylformamide

Analysis: Titrate with *Titrant* potentiometrically using a suitable electrode. [NOTE—A suitable electrode may be 6.0229.100, 0–14 pH, 70°, lithium chloride saturated in alcohol.]Perform a blank determination, and make any necessary correction.

Calculate the percentage of tartaric acid in the portion of Metaraminol Bitartrate taken:

$$\text{Result} = \{[(V_S - V_B) \times N \times F]/▲(2 \times W)▲_{\text{(ERR 1-Feb-2023)}}\} \times 100$$

V_S = *Titrant* volume consumed by the *Sample solution* (mL)

V_B = *Titrant* volume consumed by the *Blank* (mL)

N = actual normality of the *Titrant* (mEq/mL)

F = equivalency factor, 150.09 mg/mEq

W = weight of Metaraminol Bitartrate in the *Sample solution* (mg)

Acceptance criteria: 44.9%–49.7% on the dried basis

• **pH** ⟨791⟩

Sample solution: 50 mg/mL of Metaraminol Bitartrate in water

Acceptance criteria: 3.2–3.5

• **LOSS ON DRYING** ⟨731⟩

Analysis: Dry at 105° for 2 h.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at controlled room temperature.

Change to read:

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Metaraminol Bitartrate RS

USP Metaraminol Related Compound A RS

(*E*)-1-[3-(Benzyloxy)phenyl]-2-(hydroxyimino)propan-1-one.

$C_{16}H_{15}NO_3$ 269.30

USP Metaraminol Related Compound B RS

2-Amino-1-[3-(benzyloxy)phenyl]propan-1-ol.

$C_{16}H_{19}NO_2$ 257.33

USP Metaraminol Enantiomer RS

3-[(1*S*,2*R*)-2-Amino-1-hydroxypropyl]phenol ▲D-tartrate▲ (ERR 1-Feb-2023) ·

$C_9H_{13}NO_2$▲ · $C_4H_6O_6$▲ (ERR 1-Feb-2023) ▲317.29▲ (ERR 1-Feb-2023)

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

Topic/Question	Contact	Expert Committee
METARAMINOL BITARTRATE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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