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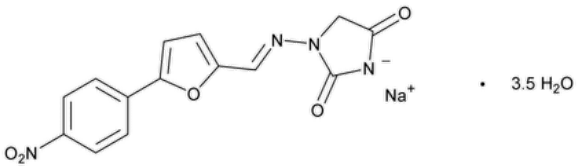
Dantrolene Sodium



$C_{14}H_9N_4NaO_5 \cdot 3½H_2O$ 399.29

2,4-Imidazolidinedione, 1-[[[5-(4-nitrophenyl)-2-furanyl]methylene]amino]-, sodium salt, hydrate (2:7);

1-[[5-(*p*-Nitrophenyl)furfurylidene]amino]hydantoin sodium salt hydrate CAS RN®: 24868-20-0; UNII: 287M0347EV.

DEFINITION

Dantrolene Sodium contains NLT 90.0% and NMT 96.0% of dantrolene ($C_{14}H_{10}N_4O_5$), the free acid form of Dantrolene Sodium, calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (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** ⟨191⟩, *Sodium*

Sample solution: To 0.1 g of Dantrolene Sodium, add 20 mL of water and 2 drops of acetic acid, shake well, and pass the resulting solution through a suitable filter. Use 2 mL of the filtrate.

Analysis

Sample: *Sample solution*

Acceptance criteria: Meets the requirements

• **D.**

Solution A: Dissolve 2.7 g of methoxyphenylacetic acid in 6 mL of tetramethylammonium hydroxide TS, and add 20 mL of dehydrated alcohol.

Solution B: 158 mg/mL of ammonium carbonate in water

Sample solution: To 0.1 g of Dantrolene Sodium, add 20 mL of water and 2 drops of acetic acid, shake well, and pass the resulting solution through a suitable filter. Use the filtrate.

Analysis

Sample: *Sample solution*

Part 1: To 0.5 mL of the *Sample solution* in a suitable container, add 1.5 mL of *Solution A*, and cool in ice water for 30 min.

Part 2: Transfer the container from *Part 1* to a water bath at 20°, and stir for 5 min.

Part 3: Add 1 mL of ammonia TS to the container from *Part 2*.

Part 4: Add 1 mL of *Solution B* to the container from *Part 3*.

Acceptance criteria: The requirements for *Part 1*, *Part 2*, *Part 3*, and *Part 4* must all be met.

Part 1: A voluminous, white, crystalline precipitate is formed.

Part 2: The precipitate does not disappear.

Part 3: The precipitate dissolves completely.

Part 4: No precipitate is formed.

ASSAY

• **Procedure**

Buffer: Dissolve 3.85 g of ammonium acetate in 1.0 L of water; adjusted with glacial acetic acid to a pH of 4.5 ± 0.1.

Solution A: Acetonitrile, *Buffer*, and water (10:20:70)

Solution B: Acetonitrile and *Buffer* (80:20)

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Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
10	60	40
20	10	90
25	10	90
25.1	90	10
35	90	10

Diluent: Acetonitrile and water (50:50)

System suitability stock solution A: 1.25 mg/mL of USP Dantrolene Sodium RS prepared as follows. Transfer a suitable amount of USP Dantrolene Sodium RS to an appropriate volumetric flask. Dissolve in 5% of the total flask volume of dimethylformamide. Add 5% of the total flask volume of glacial acetic acid, and dilute with acetone to volume.

System suitability stock solution B: 0.125 mg/mL each of USP Dantrolene Related Compound B RS and USP Dantrolene Related Compound C RS prepared as follows. Transfer suitable amounts of USP Dantrolene Related Compound B RS and USP Dantrolene Related Compound C RS to an appropriate volumetric flask. Dissolve in 5% of the total flask volume of dimethylformamide. Add 5% of the total flask volume of glacial acetic acid, and dilute with acetone to volume.

System suitability solution: 125 µg/mL of USP Dantrolene Sodium RS from *System suitability stock solution A* and 2.5 µg/mL each of USP Dantrolene Related Compound B RS and USP Dantrolene Related Compound C RS from *System suitability stock solution B* in *Diluent*

Standard stock solution: 1.0 mg/mL of USP Dantrolene RS prepared as follows. Transfer a suitable amount of USP Dantrolene RS to an appropriate volumetric flask. Dissolve in 5% of the total flask volume of dimethylformamide. Add 5% of the total flask volume of glacial acetic acid, and dilute with acetone to volume.

Standard solution: 100 µg/mL of USP Dantrolene RS from *Standard stock solution* in *Diluent*

Sample stock solution: 1.25 mg/mL of Dantrolene Sodium prepared as follows. Transfer a suitable amount of Dantrolene Sodium to an appropriate volumetric flask. Dissolve in 5% of the total flask volume of dimethylformamide. Add 5% of the total flask volume of glacial acetic acid, and dilute with acetone to volume.

Sample solution: 125 µg/mL of Dantrolene Sodium from *Sample stock solution* in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 365 nm

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

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for dantrolene related compound B, dantrolene, and dantrolene related compound C are 0.68, 1.0, and 1.24, respectively.]

Suitability requirements

Resolution: NLT 8 between dantrolene related compound C and dantrolene, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of dantrolene ($C_{14}H_{10}N_4O_5$) in the portion of Dantrolene Sodium taken:

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

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

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

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

C_U = concentration of Dantrolene Sodium in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–96.0% on the anhydrous basis

IMPURITIES

• **Limit of Dantrolene Related Compound A**

Mobile phase: Acetonitrile and water (80:20)

Standard stock solution: 17.5 µg/mL of USP Dantrolene Related Compound A RS and 50 µg/mL of USP Dantrolene Sodium RS in dimethylformamide

Standard solution: 0.35 µg/mL of USP Dantrolene Related Compound A RS and 1 µg/mL of USP Dantrolene Sodium RS from *Standard stock solution* in acetonitrile

Sample stock solution: 1.25 mg/mL of Dantrolene Sodium prepared as follows. Transfer a suitable amount of Dantrolene Sodium to an appropriate volumetric flask. Dissolve in 5% of the total flask volume of dimethylformamide. Add 5% of the total flask volume of glacial acetic acid, and dilute with acetone to volume.

Sample solution: 175 µg/mL of Dantrolene Sodium from *Sample stock solution* in acetonitrile

Chromatographic system

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

Mode: LC

Detector: UV 365 nm

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

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[Note—The dantrolene peak elutes at void volume at approximately 1.5 min.]

Suitability requirements

Tailing factor: NMT 1.5 for dantrolene related compound A

Relative standard deviation: NMT 5% for dantrolene related compound A

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of dantrolene related compound A in the portion of Dantrolene Sodium taken:

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

r_U = peak response of dantrolene related compound A from the *Sample solution*

r_S = peak response of dantrolene related compound A from the *Standard solution*

C_S = concentration of USP Dantrolene Related Compound A RS in the *Standard solution* (µg/mL)

C_U = concentration of Dantrolene Sodium in the *Sample solution* (µg/mL)

Acceptance criteria: NMT 0.15%

• **Organic Impurities**

Mobile phase, Diluent, System suitability stock solution B, System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution A: Use the *Standard solution* from the *Assay*.

Standard solution B: 0.25 µg/mL each of USP Dantrolene Related Compound B RS and USP Dantrolene Related Compound C RS from *System suitability stock solution B* in *Diluent*

System suitability

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

[Note—The relative retention times for dantrolene related compound B, dantrolene, and dantrolene related compound C are 0.68, 1.0, and 1.24, respectively.]

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Suitability requirements

Resolution: NLT 8 between dantrolene related compound C and dantrolene, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution A*

Relative standard deviation: NMT 1.0%, *Standard solution A*

Analysis

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

Calculate the percentage of dantrolene related compound B and dantrolene related compound C in the portion of Dantrolene Sodium taken:

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

r_U = peak response of dantrolene related compound B or dantrolene related compound C from the *Sample solution*

r_S = peak response of dantrolene related compound B or dantrolene related compound C from *Standard solution B*

C_S = concentration of USP Dantrolene Related Compound B RS or USP Dantrolene Related Compound C RS in *Standard solution B* (µg/mL)

C_U = concentration of Dantrolene Sodium in the *Sample solution* (µg/mL)

Acceptance criteria

Dantrolene related compound B: NMT 0.50%

Dantrolene related compound C: NMT 0.30%

SPECIFIC TESTS

• **Water Determination ⟨921⟩, *Method Ia*:** 14.5%–17.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at room temperature.

• **USP Reference Standards ⟨11⟩**

USP Dantrolene RS

1-({[5-(4-Nitrophenyl)furan-2-yl]methylene}amino)imidazolidine-2,4-dione.

$C_{14}H_{10}N_4O_5$ 314.25

USP Dantrolene Sodium RS

USP Dantrolene Related Compound A RS

1,2-Bis{[5-(4-nitrophenyl)furan-2-yl]methylene}hydrazine;
Also known as 5-(4-Nitrophenyl)furaldehyde azine.

$C_{22}H_{14}N_4O_6$ 430.38

USP Dantrolene Related Compound B RS

N-Carbamoyl-*N*-({[5-(4-nitrophenyl)furan-2-yl]methylene}amino)glycine;
Also known as 5-(4-Nitrophenyl)-2-furaldehyde-2-carboxymethyl semicarbazone.

$C_{14}H_{12}N_4O_6$ 332.27

USP Dantrolene Related Compound C RS

5-(4-Nitrophenyl)furan-2-carbaldehyde.

$C_{11}H_7NO_4$ 217.18

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DANTROLENE SODIUM	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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