Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-30801F50-510E-4C11-AC8A-1593689C571C_3_en-US
DOI: https://doi.org/10.31003/USPNF_M22070_03_01
DOI Ref: w8rfq

Dantrolene Sodium Capsules

» Dantrolene Sodium Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of dantrolene sodium ($C_{14}H_9N_4NaO_5 \cdot 3½H_2O$).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—

USP Dantrolene RS

USP Dantrolene Related Compound B RS

5-(4-Nitrophenyl)-2-furaldehyde-2-carboxymethyl semicarbazone.

$C_{14}H_{12}N_4O_6$

USP Dantrolene Sodium RS

Identification—

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

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay.*

Dissolution ⟨711⟩—

Medium: 0.5% methylbenzethonium chloride in water, pH 6.8 (adjusted with 0.1 N potassium hydroxide or 0.1 N hydrochloric acid); 900 mL, deaerated.

Apparatus 1: 100 rpm.

Time: 40 minutes.

Determine the amount of $C_{14}H_9N_4NaO_5 \cdot 3½H_2O$ dissolved by employing the following method.

Standard solution 1 (for Capsules labeled to contain 100 mg)—Transfer 25 mg of USP Dantrolene RS, accurately weighed, to a 250-mL volumetric flask. Dissolve in 5.0 mL of dimethylformamide. Add 200 mL of *Medium* and 10.0 mL of 0.1 N potassium hydroxide. Mix, dilute with *Medium* to volume, and mix. Pass through a 0.45-µm polytetrafluoroethylene (PTFE) filter, previously wetted with a few drops of isopropyl alcohol, discarding the first 5 mL.

Standard solution 2 (for Capsules labeled to contain 50 mg)—Transfer 25.0 mL of *Standard solution 1* to a 50-mL volumetric flask containing 0.5 mL of 0.1 N potassium hydroxide. Dilute with *Medium* to volume, and mix. Pass through a 0.45-µm PTFE filter, previously wetted with a few drops of isopropyl alcohol, discarding the first 5 mL.

Standard solution 3 (for Capsules labeled to contain 25 mg)—Transfer 25.0 mL of *Standard solution 1* to a 100-mL volumetric flask containing 1.0 mL of 0.1 N potassium hydroxide. Dilute with *Medium* to volume, and mix. Pass through a 0.45-µm PTFE filter, previously wetted with a few drops of isopropyl alcohol, discarding the first 5 mL.

Test solution—Withdraw 10 mL of the solution under test. Pass through a 0.45-µm PTFE filter, previously wetted with a few drops of isopropyl alcohol. Discard the first 5 mL. Collect the filtered solution in a tube that contains 1 drop of 1 N potassium hydroxide, and mix.

System suitability—[Note—All absorbance values should be obtained on solutions within 2 hours of their preparation.] Using a 0.1-cm cell, measure the absorbance of the *Medium,* using water as the blank, and measure the absorbance of each of the three *Standard solutions* using *Medium* as the blank, at the wavelength of maximum absorbance at about 395 nm. The system is considered suitable for use if the following criteria are met: the absorbance of the *Medium* is less than 10% of the absorbance of *Standard solution 1;* the absorbance of *Standard solution 2* is between 0.3 and 0.5; and the ratio of the absorbance of *Standard solution 1* to that of *Standard solution 3* is 4.00 ± 0.10.

Determine the amount of $C_{14}H_9N_4NaO_5 \cdot 3½H_2O$ dissolved by measuring the absorbance of the *Test solution* at the wavelength of maximum absorbance at about 395 nm in comparison with the appropriate *Standard solution,* using a 0.1-cm cell and *Medium* as the blank. All absorbance values are obtained on solutions within 2 hours of their preparation. Calculate the percentage of $C_{14}H_9N_4NaO_5 \cdot 3½H_2O$ dissolved by the formula:

$$\frac{A_U \times C_S \times 900 \times 100}{A_S \times 0.79186 \times LC}$$

in which A_U and A_S are the absorbances obtained from the *Test solution* and the *Standard solution*, respectively; C_S is the concentration, in mg per mL, of dantrolene in the *Standard solution;* 900 is the volume, in mL, of *Medium;* 100 is the conversion factor to percentage; 0.79186 is the correction for water of hydration and sodium contained in the dantrolene sodium monohydrate form of the drug, assuming that the bulk drug contains 15% of water and 6.84% of sodium; and *LC* is the Capsule label claim, in mg.

Tolerances—Not less than 75% (*Q*) of the labeled amount of $C_{14}H_9N_4NaO_5 \cdot 3½H_2O$ is dissolved in 40 minutes.

Uniformity of dosage units ⟨905⟩**:** meet the requirements.

Related compounds—

Diluent, Solution A, Solution B, Mobile phase, and *Chromatographic system*—Proceed as directed in the *Assay.*

Standard solution—Transfer 5 mg, accurately weighed, of USP Dantrolene Related Compound B RS into a 50-mL volumetric flask, and dissolve in 2.5 mL of dimethylformamide. Add 2.5 mL of glacial acetic acid, and dilute with acetone to volume. The final concentration is about 0.1 mg per mL. Quantitatively dilute this solution with *Diluent* to obtain a solution having a known concentration of about 0.0005 mg per mL of dantrolene related compound B.

Test solution—Use the *Assay preparation.*

Procedure—Inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of dantrolene related compound B in the portion of Capsules taken by the formula:

$$100(r_U/r_S)(C_S/C_T)$$

in which r_U is the individual peak response for dantrolene related compound B obtained from the *Test solution;* r_S is the response of the corresponding peak in the *Standard solution;* C_S is the concentration, in mg per mL, of dantrolene related compound B in the *Standard solution*; and C_T is the concentration, in mg per mL, of dantrolene sodium in the *Test solution:* not more than 2% of dantrolene related compound B is found.

Assay—

Diluent—Prepare a solution of acetonitrile and water (70:30).

Buffer solution—Dissolve 3.3 g of ammonium acetate in 1 L of water.

Solution A—Prepare a filtered and degassed mixture of *Buffer solution,* acetonitrile, and glacial acetic acid (120:76:7).

Solution B—Prepare a filtered and degassed mixture of acetonitrile and water (70:30).

Mobile phase—Use variable mixtures of *Solution A* and *Solution B,* as directed for *Chromatographic system.* Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

System suitability solution—Use the *Standard solution,* prepared as directed in the test for *Related compounds.*

Standard preparation—Transfer 40 mg, accurately weighed, of USP Dantrolene RS to a 50-mL volumetric flask, and dissolve in 2.5 mL of dimethylformamide. Add 2.5 mL of glacial acetic acid, and dilute with acetone to volume. The final concentration is about 0.8 mg per mL. Quantitatively dilute this solution with *Diluent* to obtain a solution having a known concentration of about 0.08 mg per mL of dantrolene.

Assay preparation—Mix the combined contents of not fewer than 20 Capsules, and transfer an accurately weighed portion, equivalent to the average weight of one Capsule, to a 50-mL volumetric flask. Add 10 mL of dimethylformamide, and sonicate for 15 minutes to dissolve. Add 5 mL of glacial acetic acid, and dilute with acetone to volume. Quantitatively dilute this solution with *Diluent* to obtain a solution having 0.1 mg per mL of dantrolene sodium, and pass through a 0.45-µm nylon filter.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 365-nm detector and a 4.6-mm ×15-cm column that contains 5-µm packing L1. The flow rate is about 1.5 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0–8	100	0	isocratic
8–8.1	100→0	0→100	linear gradient
8.1–13	0	100	isocratic
13–13.1	0→100	100→0	linear gradient
13.1–20	100	0	re-equilibration

Separately inject the *System suitability solution* and the *Standard preparation* into the chromatograph, record the chromatograms, and measure the peak responses as directed for *Procedure:* the tailing factor is not more than 1.5; and the relative standard deviation for replicate injections for dantrolene is not more than 1.0%.

[Note—For the purpose of peak identification, the approximate relative retention times are 0.68 for dantrolene related compound B and 1.0 for dantrolene.]

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the dantrolene peaks. Calculate the percentage of dantrolene sodium ($C_{14}H_9N_4NaO_5 \cdot 3½H_2O$) in the portion of Capsules taken by the formula:

$$100(399.29/314.25)(r_U/r_S)(C_S/C_U)$$

in which 399.29 is the molecular weight of dantrolene sodium; 314.25 is the molecular weight of dantrolene; r_U and r_S are the peak responses for dantrolene obtained from the *Assay preparation* and the *Standard preparation,* respectively; C_S is the concentration, in mg per mL, of

dantrolene in the *Standard preparation;* and C_U is the concentration, in mg per mL, of dantrolene sodium ($C_{14}H_9N_4NaO_5 \cdot 3½H_2O$) in the *Assay preparation.*

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

Topic/Question	Contact	Expert Committee
DANTROLENE SODIUM CAPSULES	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 34(5)

Current DocID: GUID-30801F50-510E-4C11-AC8A-1593689C571C_3_en-US
Previous DocID: GUID-30801F50-510E-4C11-AC8A-1593689C571C_2_en-US
DOI: https://doi.org/10.31003/USPNF_M22070_03_01
DOI ref: w8rfq