Edition: BP 2025 (Ph. Eur. 11.6 update)

Dantrolene Sodium

General Notices

C₁₄H₉N₄NaO₅,3½H₂O 399.3 24868-20-0

Action and use

Skeletal muscle relaxant.

Preparation

Dantrolene Oral Suspension

DEFINITION

Dantrolene Sodium is 1-(5-p-nitrophenylfurfurylideneamino)hydantoin sodium. It contains not less than 98.0% and not more than 102.0% of $C_{14}H_9N_4NaO_5$, calculated with reference to the anhydrous substance.

CHARACTERISTICS

A yellowish-orange to orange crystalline powder.

Very slightly soluble in <u>water</u>; slightly soluble in <u>ethanol (96%)</u>; sparingly soluble in <u>methanol</u>; practically insoluble in <u>acetone</u>.

IDENTIFICATION

- A. The <u>infrared absorption spectrum</u>, <u>Appendix II A</u>, is concordant with the *reference spectrum* of dantrolene sodium (<u>RS 422</u>).
- B. In the Assay, the chromatogram obtained with solution (1) shows a peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).
- C. To 0.1 g of the substance being examined add 20 mL of <u>water</u> and 2 drops of <u>acetic acid</u>, shake well and filter. The filtrate yields the reactions characteristic of <u>sodium salts</u>, <u>Appendix VI</u>.

TESTS

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Shake 0.7 g in 10 mL of <u>water</u> for 5 minutes and centrifuge. To 5 mL of the supernatant add 45 mL of <u>water</u> and 3 drops of <u>phenolphthalein solution R1</u> and 0.1 mL of <u>0.1m hydrochloric acid VS</u>. A red colour is not produced.

Related substances

Carry out the method for <u>liquid chromatography</u>, <u>Appendix III D</u>, using the following solutions.

- (1) Dissolve 50 mg of the substance being examined in 20 mL of <u>tetrahydrofuran</u> and 2 mL of <u>glacial acetic acid</u> and dilute with sufficient <u>absolute ethanol</u> to produce 100 mL.
- (2) Dilute 1 mL of solution (1) to 100 mL with absolute ethanol.
- (3) Dissolve 5 mg of <u>dantrolene sodium BPCRS</u> and 0.1 g of <u>theophylline BPCRS</u> in 20 mL of <u>tetrahydrofuran</u> and 2 mL of <u>glacial acetic acid</u> and dilute with sufficient <u>absolute ethanol</u> to produce 100 mL. Further dilute 10 mL of this solution to 100 mL with <u>absolute ethanol</u>.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (15 cm \times 4.6 mm) packed with <u>silica gel for chromatography</u> (5 μ m) (Zorbax Sil is suitable).
- (b) Use isocratic elution and the mobile phase described below.
- (c) Adjust the flow rate of the mobile phase so that the retention time of the peak corresponding to Dantrolene Sodium is about 8 minutes.
- (d) Use a column temperature of 30°.
- (e) Use a detection wavelength of 300 nm.
- (f) Inject 10 μL of each solution.
- (g) For solution (1) allow the chromatography to proceed for at least twice the retention time of the principal peak.

MOBILE PHASE

9 volumes of *absolute ethanol*, 10 volumes of *glacial acetic acid* and 90 volumes of *hexane*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the <u>resolution</u> between the peaks corresponding to the ophylline and dantrolene is at least 6.

LIMITS

In the chromatogram obtained with solution (1):

the total area of all the <u>secondary peaks</u> is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%).

Water

14.5 to 17.0% w/w, Appendix IX C. Use 0.2 g

ASSAY

Carry out the method for <u>liquid chromatography</u>, <u>Appendix III D</u>, using the following solutions.

- (1) Dissolve 60 mg of the substance being examined in 50 mL of <u>dimethylformamide</u> and dilute 1 volume of the resulting solution to 100 volumes with the mobile phase.
- (2) Dilute 1 volume of a 0.12% w/v solution of <u>dantrolene sodium BPCRS</u> in <u>dimethylformamide</u> to 100 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (15 cm × 4.6 mm) packed with spherical particles of silica, 5 μm in diameter, the surface of which has been modified with chemically-bonded nitrile groups (Spherisorb CN is suitable).
- (b) Use isocratic elution and the mobile phase described below.
- (c) Use a flow rate of 1 mL per minute.
- (d) Use an ambient column temperature.
- (e) Use a detection wavelength of 262 nm.

https://nhathuocngocanh.com/bp/ (f) Inject 20 µL of each solution.

MOBILE PHASE

15 volumes of <u>acetonitrile</u> and 85 volumes of a phosphate buffer pH 6.8 prepared by dissolving 11.88 g of <u>disodium</u> <u>hydrogen orthophosphate</u> and 9.08 g of <u>potassium dihydrogen orthophosphate</u> in 1000 mL of <u>water</u>.

DETERMINATION OF CONTENT

 $Calculate \ the \ content \ of \ C_{14}H_9N_4NaO_5 \ in \ the \ substance \ being \ examined \ using \ the \ declared \ content \ of \ C_{14}H_9N_4NaO_5 \ in$ dantrolene sodium BPCRS.