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Anagrelide Capsules

DEFINITION

Anagrelide Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of anagrelide ($C_{10}H_7Cl_2N_3O$).

IDENTIFICATION

- A.** The UV absorption spectrum of the major peak of the *Sample solution* exhibits maxima and minima at the same wavelengths as those of the corresponding peak of the *Standard solution*, as obtained in the Assay.
- 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: 1.0 g/L of [sodium hexanesulfonate](#). Add 1.0 mL of [phosphoric acid](#) and filter.

Mobile phase: [Acetonitrile](#) and *Solution A* (7:13)

Diluent: [Acetonitrile](#) and [water](#) (1:1)

Standard stock solution: 0.25 mg/mL of [USP Anagrelide Hydrochloride RS](#) in [acetonitrile](#). Initially add [acetonitrile](#) (about 80% of the volume of the flask) and a small quantity of 2 N [hydrochloric acid](#) (about 0.2 mL for every 100 mL of the final volume). Sonicate to dissolve, and dilute with [acetonitrile](#) to volume.

Standard solution: 0.01 mg/mL of anagrelide free base in *Diluent* from *Standard stock solution*

Sample solution: Nominally 0.01 mg/mL of anagrelide free base prepared from the contents of NLT 20 Capsules. Add *Diluent* (80% of the volume of the flask), sonicate for 10 min, and stir for 15 min. Further dilute with *Diluent* to volume, centrifuge for 15 min at 4000 rpm, and use the supernatant for analysis.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 4-μm packing L11

Column temperature: 60°

Flow rate: 1.0 mL/min

Injection volume: 20 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of anagrelide ($C_{10}H_7Cl_2N_3O$) in the portion of Capsules taken:

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

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

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

C_S = concentration of anagrelide in the *Standard solution* (mg/mL)

C_U = nominal concentration of anagrelide in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\)](#)

Medium: 0.1 N [hydrochloric acid](#); 900 mL

Apparatus 1: 100 rpm

Time: 15 min

Mobile phase: Prepare as directed in the Assay.

Standard solution: Transfer about 30.32 mg of [USP Anagrelide Hydrochloride RS](#), equivalent to 25.00 mg of anagrelide, to a 100-mL volumetric flask. Add about 80 mL of [acetonitrile](#) and 3 drops of 2 N [hydrochloric acid](#). Sonicate until dissolved. Dilute with [acetonitrile](#) to volume. Dilute this solution with *Medium* to obtain a final concentration of about $(L/1000)$ mg/mL, where L is the label claim in mg/Capsule.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45- μ m pore size.

Chromatographic system

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

Mode: LC

Detector: UV 274 nm

Column: 4.6-mm $\times$ 15-cm; 5- μ m packing L7

Sample cooler temperature: 5°

Flow rate: 1.0 mL/min

Injection volume: 20 μ L

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of anagrelide dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \blacktriangle (\text{ERR 1-Oct-2019}) \times (M_{r1}/M_{r2}) \times (V/L) \times 100$$

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

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

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

$\blacktriangle$ (ERR 1-Oct-2019)

M_{r1} = molecular weight of anagrelide, 256.09

M_{r2} = molecular weight of anagrelide hydrochloride, 292.55

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

Tolerances: NLT 80% (Q) of the labeled amount of anagrelide is dissolved.

- [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meet the requirements

IMPURITIES

• ORGANIC IMPURITIES

Buffer: 6.8 g/L of [monobasic potassium phosphate](#). Adjust with diluted [phosphoric acid](#) to a pH of 3.50 ± 0.05 . Mix well and filter.

Mobile phase: [Acetonitrile](#) and *Buffer* (27:73)

Diluent: [Acetonitrile](#) and [water](#) (7:13)

Related compound A stock solution: 10 μ g/mL of [USP Anagrelide Related Compound A RS](#) in *Diluent*

Related compound C stock solution: 10 μ g/mL of [USP Anagrelide Related Compound C RS](#) in *Diluent*

System suitability solution: 0.2 μ g/mL each of [USP Anagrelide Related Compound A RS](#) and [USP Anagrelide Related Compound C RS](#) and 0.02 mg/mL of [USP Anagrelide Hydrochloride RS](#) prepared as follows. Initially dissolve [USP Anagrelide Hydrochloride RS](#) in *Diluent* (about 80% of the volume of the flask), sonicate for 10 min, and stir for 15 min. Add appropriate quantities of *Related compound A stock solution* and *Related compound C stock solution*, and dilute with *Diluent* to volume.

Standard stock solution: Prepare as directed in the Assay.

Standard solution: 0.10 μ g/mL of anagrelide free base in *Diluent* from *Standard stock solution*

Sample solution: Nominally 0.02 mg/mL of anagrelide free base from NLT 20 Capsules. Initially add *Diluent* to about 80% of the volume of the flask, sonicate for 10 min, stir for about 15 min, and dilute with *Diluent* to volume. Centrifuge the solution at about 4000 rpm for 15 min, and use the supernatant for analysis.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm