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Spironolactone Tablets

DEFINITION
Spironolactone Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of spironolactone ($C_{24}H_{32}O_4S$).

IDENTIFICATION

Change to read:

• **A.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Aug-2021)

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Aug-2021)

ASSAY

Change to read:

• **Procedure**

Mobile phase: Methanol and water (60:40)

Diluent: Acetonitrile and water (50:50)

Standard solution: 0.5 mg/mL of USP Spironolactone RS in *Diluent*

Sample stock solution: Nominally 1 mg/mL of spironolactone in *Diluent* prepared as follows. Weigh NLT 10 Tablets, and transfer to a suitable volumetric flask. ▲▲ (USP 1-Aug-2021) Add a sufficient quantity of *Diluent*, shake for about 30 min, and sonicate for 30 min or until the Tablets are disintegrated. Cool the solution to room temperature, dilute with *Diluent* to volume, and centrifuge a suitable portion of the mixture.

Sample solution: Nominally 0.5 mg/mL of spironolactone in *Diluent* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm. ▲For *Identification B*, use a diode array detector in the range of 210–400 nm.▲ (USP 1-Aug-2021)

Column: 4.6-mm × 15-cm; ▲5-µm▲ (USP 1-Aug-2021) packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 2 times the retention time of spironolactone▲ (USP 1-Aug-2021)

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of spironolactone ($C_{24}H_{32}O_4S$) in the portion of Tablets taken:

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

r_U = peak response ▲of spironolactone▲ (USP 1-Aug-2021) from the *Sample solution*

r_S = peak response ▲of spironolactone▲ (USP 1-Aug-2021) from the *Standard solution*

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

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

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid containing 0.1% of sodium dodecyl sulfate; 1000 mL

Apparatus 2: 75 rpm

Time: 60 min

Standard solution: A known concentration of USP Spironolactone RS in *Medium*. [Note—A volume of alcohol not exceeding 1% of the final volume of the solution may be used to prepare the *Standard solution*.]

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium*, as necessary in comparison with the *Standard solution*.

Instrumental conditions

▲(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)▲ (USP 1-Aug-2021)

Mode: UV

Analytical wavelength: 242 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the ▲percentage of the labeled▲ (USP 1-Aug-2021) amount of spironolactone ($C_{24}H_{32}O_4S$) dissolved:

$$▲\text{Result} = (A_U/A_S) \times C_S \times D \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor for the *Sample solution*

V = volume of *Medium*, 1000 mL

L = label claim of spironolactone (mg/Tablet)

▲ (USP 1-Aug-2021)

Tolerances: NLT 75% (Q) of the labeled amount of spironolactone ($C_{24}H_{32}O_4S$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

Add the following:

▲IMPURITIES

• **Organic Impurities**

Diluent: Acetonitrile and water (50:50)

Mobile phase: Acetonitrile, tetrahydrofuran, methanol, and water (15:20:425:540)

Standard stock solution A: 100 µg/mL of USP Spironolactone RS prepared as follows. Dissolve a suitable amount of USP Spironolactone RS in a suitable volumetric flask in about 10% of the total volume with tetrahydrofuran. Dilute with *Diluent* to volume.

Standard stock solution B: 100 µg/mL of USP Spironolactone Related Compound A RS prepared as follows. Dissolve a suitable amount of USP Spironolactone Related Compound A RS in a suitable volumetric flask in about 10% of the total volume with tetrahydrofuran. Dilute with *Diluent* to volume.

Sensitivity solution: 2 µg/mL of USP Spironolactone RS in *Diluent*, from *Standard stock solution A*

Standard solution: 4 µg/mL each of USP Spironolactone RS and USP Spironolactone Related Compound A RS in *Diluent*, from *Standard stock solution A* and *Standard stock solution B*

Sample solution: Nominally 2 mg/mL of spironolactone in *Diluent* prepared as follows. Transfer a suitable number of Tablets into a volumetric flask. Add about 10% of the total volume of tetrahydrofuran and swirl to disintegrate. Add NLT 80% of the total volume of *Diluent*. Shake by mechanical means for 30 min. Follow by sonication for 30 min and then cool to room temperature. Dilute with *Diluent* to volume. Centrifuge and use the supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Column temperature: 40°

Flow rate: 1.0 mL/min

Injection volume: 20 µL

Run time: NLT 2.5 times the retention time of spironolactone

System suitability

Samples: *Sensitivity solution* and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between spironolactone and spironolactone related compound A, *Standard solution*

Relative standard deviation: NMT 5.0% for spironolactone and spironolactone related compound A, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of spironolactone related compound A in the portion of Tablets taken:

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

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

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

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

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

Calculate the percentage of any unspecified degradation product in the portion of Tablets taken:

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

r_U = peak response of any unspecified degradation product from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 1*. The reporting threshold is 0.1%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Spironolactone	1.0	—
Spironolactone related compound A	1.2	1.0
Any unspecified degradation product	—	0.2
Total degradation products	—	2.0▲ (USP 1-Aug-2021)

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight, light-resistant containers. ▲Store at controlled room temperature.▲ (USP 1-Aug-2021)

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Spironolactone RS

▲ USP Spironolactone Related Compound A RS

(2′*R*)-3′,4′-Dihydro-5′*H*-spiro[androst-4,6-diene-17,2′-furan]-3,5′-dione.

$C_{22}H_{28}O_3$ 340.46▲ (USP 1-Aug-2021)

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

Topic/Question	Contact	Expert Committee
SPIRONOLACTONE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

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