

Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Dec-2023
Document Type: USP Monographs
DocId: GUID-0BD3E17A-B017-4673-95C5-772F72CA4CF9_2_en-US
DOI: https://doi.org/10.31003/USPNF_M77920_02_01
DOI Ref: q13vc

© 2025 USPC
Do not distribute

Spironolactone and Hydrochlorothiazide Tablets

DEFINITION
Spironolactone and Hydrochlorothiazide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amounts of spironolactone ($C_{24}H_{32}O_4S$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$).

IDENTIFICATION

- **A.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.

Add the following:

- ▲• **B.** The UV spectra of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.▲ (USP 1-Dec-2023)

ASSAY

Change to read:

- **PROCEDURE**

▲Protect all solutions containing spironolactone and hydrochlorothiazide from light.

Solution A: [Methanol](#) and [water](#) (10:90)

Solution B: [Methanol](#)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
5	100	0
6	59	41
26	59	41
26.05	100	0
30	100	0

Diluent: [Acetonitrile](#) and [water](#) (50:50)

System suitability stock solution: 50 µg/mL each of [USP Spironolactone Related Compound A RS](#) and [USP Benzothiadiazine Related Compound A RS](#) in *Diluent*. Sonicate to dissolve if necessary.

System suitability solution: 0.1 mg/mL each of [USP Spironolactone RS](#) and [USP Hydrochlorothiazide RS](#), and 1 µg/mL each of [USP Spironolactone Related Compound A RS](#) and [USP Benzothiadiazine Related Compound A RS](#) in *Diluent* prepared as follows. Transfer an appropriate amount of [USP Spironolactone RS](#) and [USP Hydrochlorothiazide RS](#) to a suitable volumetric flask. Add a suitable portion of the *System suitability stock solution* and dilute with *Diluent* to volume.

Standard solution: 0.1 mg/mL each of [USP Spironolactone RS](#) and [USP Hydrochlorothiazide RS](#) in *Diluent*. Sonicate to dissolve if necessary.

Sample stock solution: Nominally 0.5 mg/mL each of spironolactone and hydrochlorothiazide from Tablets prepared as follows. Transfer Tablets (NLT 10) to a suitable volumetric flask. Add *Diluent* to about 60% of the flask volume, sonicate for about 10 min, and maintain a cool

sonication bath temperature. Shake for about another 30 min and allow to cool to room temperature. Dilute with *Diluent* to volume.

Sample solution: Nominally 0.1 mg/mL each of spironolactone and hydrochlorothiazide from the *Sample stock solution* prepared as follows.

Transfer 10.0 mL of the *Sample stock solution* to a 50-mL volumetric flask. Dilute with *Diluent* to volume. Pass a portion through a suitable filter of 0.45-µm pore size and discard the first 4 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. For *Identification B*, use a diode array detector in the range of 190–400 nm.

Column: 4.6-mm × 15-cm; 2.7-µm packing [L1](#)

Temperatures

Autosampler: 5°

Column: 40°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE—The relative retention times for benzothiadiazine related compound A, hydrochlorothiazide, spironolactone, and spironolactone related compound A are 0.7, 1.0, 4.0, and 4.4, respectively.]

Suitability requirements

Resolution: NLT 2.0 between benzothiadiazine related compound A and hydrochlorothiazide; NLT 2.0 between spironolactone and spironolactone related compound A, *System suitability solution*

Tailing factor: NMT 2.0 for hydrochlorothiazide and spironolactone, *Standard solution*

Relative standard deviation: NMT 1.0% for hydrochlorothiazide and spironolactone, *Standard solution* ▲ (USP 1-Dec-2023)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentages of ▲the labeled amounts ▲ (USP 1-Dec-2023) of spironolactone ($C_{24}H_{32}O_4S$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) 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 or hydrochlorothiazide from the *Sample solution*

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

C_S = concentration of [USP Spironolactone RS](#) or [USP Hydrochlorothiazide RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of spironolactone or hydrochlorothiazide 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](#) containing 0.1% [sodium dodecyl sulfate](#); 900 mL

Apparatus 2: 75 rpm

Time: 60 min

Solution A: [Acetonitrile](#)

Solution B: 4.5 g/L of [monobasic potassium phosphate](#) in [water](#)

Mobile phase: See [Table 2](#).

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	25	75



Documents

Document Sharing Hub