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Spironolactone and Hydrochlorothiazide Compounded Oral Suspension

DEFINITION

Spironolactone and Hydrochlorothiazide Compounded Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of spironolactone ($C_{24}H_{32}O_4S$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$).

Prepare an oral suspension containing 5 mg/mL of spironolactone and 5 mg/mL of hydrochlorothiazide as follows (see *Pharmaceutical Compounding—Nonsterile Preparations ⟨795⟩*).

Spironolactone and Hydrochlorothiazide tablets[a] equivalent to	500 mg of spironolactone and 500 mg of hydrochlorothiazide
Vehicle: a 1:1 mixture of Ora-Sweet[b] (regular or sugar-free) and Ora-Plus,[b] a sufficient quantity to make	100 mL

[a] Spironolactone and hydrochlorothiazide 25-mg/25-mg tablets, Mylan Pharmaceutical Inc., Morgantown, WV.

[b] Paddock Laboratories, Minneapolis, MN.

Calculate the required quantity of each ingredient for the total amount to be prepared. Place the required number of *Spironolactone and Hydrochlorothiazide tablets* in a suitable mortar, and comminute to a fine powder. Add the *Vehicle* in small portions, and triturate to make a smooth paste. Add increasing volumes of the *Vehicle* to make a spironolactone and hydrochlorothiazide liquid that is pourable. Transfer the contents of the mortar, stepwise and quantitatively, to a calibrated bottle. Add enough of the *Vehicle* to bring to final volume, and mix well.

ASSAY

• **Procedure**

Mobile phase: Methanol and water (70:30). Filter and degas.

Standard solution: 0.1 mg/mL of USP Spironolactone RS and 0.1 mg/mL of USP Hydrochlorothiazide RS in methanol

Sample solution: Shake thoroughly by hand each bottle of Oral Suspension. Prepare 0.1 mg/mL of spironolactone and 0.1 mg/mL of hydrochlorothiazide from Oral Suspension and methanol. Centrifuge.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.0 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[Note—The retention times for hydrochlorothiazide and spironolactone are about 3.5 and 7.4 min, respectively.]

Suitability requirements

Relative standard deviation: NMT 2.0% for spironolactone and NMT 2.0% for hydrochlorothiazide for replicate injections

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 Oral Suspension taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response 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)

Calculate the percentage of the labeled amount of hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) in the portion of Oral Suspension taken by the same formula, changing the terms to refer to hydrochlorothiazide.

Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 3.8–4.8

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Package in tight, light-resistant containers. Store in a refrigerator or at controlled room temperature.

• **Beyond-Use Date:** NMT 60 days after the date on which it was compounded, when stored in a refrigerator or controlled at room temperature

• **Labeling:** Label it to indicate that it is to be well shaken before use, and to state the *Beyond-Use Date*.

• **USP Reference Standards** ⟨11⟩

USP Hydrochlorothiazide RS

USP Spironolactone RS

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

Topic/Question	Contact	Expert Committee
SPIRONOLACTONE AND HYDROCHLOROTHIAZIDE COMPOUNDED ORAL SUSPENSION	Brian Serumaga Science Program Manager	CMP2020 Compounding 2020
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CMP2020 Compounding 2020

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