Status: Currently Official on 16-Feb-2025
Official Date: Official Prior to 2013
Document Type: USP Monographs
DocId: GUID-16DB5C9D-F775-46BC-B209-46A80472A608_1_en-US
DOI: https://doi.org/10.31003/USPNF_M79300_01_01
DOI Ref: fe91s

Sulfamethoxazole and Trimethoprim Tablets

DEFINITION

Sulfamethoxazole and Trimethoprim Tablets contain NLT 93.0% and NMT 107.0% of the labeled amounts of sulfamethoxazole ($C_{10}H_{11}N_3O_3S$) and trimethoprim ($C_{14}H_{18}N_4O_3$).

IDENTIFICATION

• **A.**

Standard solution A: 0.4 mg/mL of USP Trimethoprim RS in methanol

Standard solution B: 2 mg/mL of USP Sulfamethoxazole RS in methanol

Sample solution: Transfer an amount of finely ground Tablets, equivalent to 4 mg of trimethoprim, to a 10-mL volumetric flask, add 8 mL of methanol, and warm for several min on a steam bath with frequent shaking. Cool, dilute with methanol to volume, and centrifuge briefly.

Chromatographic system

Mode: TLC

Application volume: 5 µL

Developing solvent system: Chloroform, isopropyl alcohol, and diethylamine (6:5:1)

Analysis

Samples: *Standard solution A*, *Standard solution B*, and *Sample solution*

Apply the *Samples* to separate points about 3 cm from one end of the plate. Dry the spots in a current of warm air, and develop the plate with *Developing solvent system* in a chamber that is lined with filter paper. Remove the plate, dry, and examine under short-wavelength UV light.

Acceptance criteria: The trimethoprim and sulfamethoxazole spots from the solution under test have the same R_F values as the spots from the corresponding *Standard solutions*.

ASSAY

• **Procedure**

Mobile phase: Mix 1400 mL of water, 400 mL of acetonitrile, and 2.0 mL of triethylamine in a 2000-mL volumetric flask. Allow to equilibrate to room temperature, and adjust with 0.2 N sodium hydroxide or dilute glacial acetic acid (1 in 100) to a pH of 5.9 ± 0.1. Dilute with water to volume, and pass through a filter of 0.45-µm pore size.

Standard stock solution: 0.32 mg/mL of USP Trimethoprim RS and 0.32*J* mg/mL of USP Sulfamethoxazole RS in methanol, where *J* is the ratio of the labeled amount, in mg, of sulfamethoxazole to the labeled amount, in mg, of trimethoprim in the dosage form

Standard solution: 0.032 mg/mL of USP Trimethoprim RS per mL and 0.032*J* mg/mL of USP Sulfamethoxazole RS per mL in *Mobile phase* from *Standard stock solution*

Sample stock solution: Transfer from finely powdered Tablets (NLT 20), an equivalent to 160 mg of sulfamethoxazole, to a 100-mL volumetric flask. Add 50 mL of methanol and sonicate, with intermittent shaking, for 5 min. Allow to equilibrate to room temperature, dilute with methanol to volume, and filter. Use the filtrate in the preparation of the *Sample solution*.

Sample solution: Nominally 0.16 mg/mL of sulfamethoxazole in *Mobile phase* from *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for trimethoprim and sulfamethoxazole are 1.0 and 1.8, respectively.]

Suitability requirements

Resolution: NLT 5.0 between sulfamethoxazole and trimethoprim

Tailing factor: NMT 2.0 for sulfamethoxazole and trimethoprim

Relative standard deviation: NMT 2.0% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of trimethoprim ($C_{14}H_{18}N_4O_3$) and sulfamethoxazole ($C_{10}H_{11}N_3O_3S$) in the portion of Tablets taken:

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

r_U = peak response of trimethoprim or sulfamethoxazole from the *Sample solution*

r_S = peak response of trimethoprim or sulfamethoxazole from the *Standard solution*

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

C_U = nominal concentration of trimethoprim or sulfamethoxazole in the *Sample solution* (mg/mL)

Acceptance criteria: 93.0%–107.0% each of sulfamethoxazole ($C_{10}H_{11}N_3O_3S$) and trimethoprim ($C_{14}H_{18}N_4O_3$)

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 75 rpm

Time: 60 min

Standard solution: USP Sulfamethoxazole RS and USP Trimethoprim RS at a known concentration

Sample solution: Pass a portion of the solution under test through a suitable filter.

Mobile phase, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amounts of sulfamethoxazole ($C_{10}H_{11}N_3O_3S$) and trimethoprim ($C_{14}H_{18}N_4O_3$) dissolved by comparison of the peak responses obtained from a filtered aliquot of the solution under test with the peak responses from the corresponding component obtained from the *Standard solution*.

Calculate the percentage of each active component dissolved

Tolerances: NLT 70% (*Q*) of the labeled amount of sulfamethoxazole ($C_{10}H_{11}N_3O_3S$) and trimethoprim ($C_{14}H_{18}N_4O_3$) is dissolved.

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

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers.

• **USP Reference Standards ⟨11⟩**

USP Sulfamethoxazole RS

USP Trimethoprim RS

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

Topic/Question	Contact	Expert Committee
SULFAMETHOXAZOLE AND TRIMETHOPRIM TABLETS	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 40(3)
Current DocID: GUID-16DB5C9D-F775-46BC-B209-46A80472A608_1_en-US
DOI: https://doi.org/10.31003/USPNF_M79300_01_01
DOI ref: fe91s