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Theophylline Capsules

» Theophylline Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of anhydrous theophylline ($C_7H_8N_4O_2$).

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—
USP Theophylline RS

Identification—

Change to read:

A: ▲Triturate a quantity of the contents of Capsules, equivalent to about 500 mg of theophylline, with 10-mL and 5-mL portions of solvent hexane, and discard the solvent hexane. Triturate the residue with two 10-mL portions of a mixture of equal volumes of 6 N ammonium hydroxide and water, and filter each time. Evaporate the combined filtrates to about 5 mL, neutralize, if necessary, with 6 N acetic acid, using litmus, and then cool to about 15°, with stirring. Collect the precipitate on a filter, wash it with cold water, and dry at 105° for 2 hours: the theophylline so obtained melts between 270° and 274° (see *Melting Range or Temperature ⟨741⟩, Procedures, Procedure for Class I*). Retain the remaining portion of the theophylline for use in *Identification* test *B*.▲ (ERR 1-Feb-2024)

Change to read:

B: ▲The IR absorption spectrum of a potassium bromide dispersion of the residue obtained in *Identification* test *A* exhibits maxima only at the same wavelengths as that of a potassium bromide dispersion of USP Theophylline RS.▲ (ERR 1-Feb-2024)

Change to read:

▲C: ▲ (ERR 1-Feb-2024) The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

Dissolution ⟨711⟩—
Medium: water; 900 mL.
Apparatus 2: 50 rpm.
Time: 60 minutes.
Procedure—Determine the amount of $C_7H_8N_4O_2$ dissolved from UV absorbances at the wavelength of maximum absorbance at about 268 nm of filtered portions of the solution under test, suitably diluted with 0.1 N hydrochloric acid, if necessary, in comparison with a Standard solution having a known concentration of USP Theophylline RS in the same medium.
Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_7H_8N_4O_2$ is dissolved in 60 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—
Mobile phase—Prepare a solution containing a mixture of water, methanol, and glacial acetic acid (64:35:1).
Standard preparation—Dissolve an accurately weighed quantity of USP Theophylline RS in methanol to obtain a solution having a known concentration of about 400 µg per mL.
Assay preparation for hard Capsules—Remove, as completely as possible, the contents of not less than 20 Capsules, weigh, and mix. Transfer an accurately weighed portion of the powder, equivalent to about 100 mg of anhydrous theophylline, to a 250-mL volumetric flask, add about 150 mL of methanol, and shake to dissolve. Dilute with methanol to volume, mix, and filter, using a membrane filter.
Assay preparation for soft Capsules—Cut open 20 Capsules, and place them in a 200-mL volumetric flask. Add 50 mL of 6 N ammonium hydroxide, shake to dissolve the contents, add water to volume, mix, and filter, discarding the first 20 mL of the filtrate. Transfer an accurately measured portion of the filtrate, equivalent to about 100 mg of anhydrous theophylline, to a 250-mL volumetric flask, add methanol to volume, mix, and filter through a membrane filter.
Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 254-nm detector and a 4-mm × 30-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph three replicate injections of the *Standard*

preparation, and record the peak responses as directed for *Procedure:* the relative standard deviation is not more than 2%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses. Calculate the quantity, in mg, of anhydrous theophylline in the portion of Capsule contents taken by the formula:

$$0.25C(r_U/r_S)$$

in which C is the concentration, in µg per mL, of USP Theophylline RS in the *Standard preparation*, and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

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

Topic/Question	Contact	Expert Committee
THEOPHYLLINE CAPSULES	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. Information currently unavailable

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