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Aminophylline Suppositories

DEFINITION

Aminophylline Suppositories contain an amount of aminophylline equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of anhydrous theophylline ($C_7H_8N_4O_2$).

IDENTIFICATION

• **A.**

Analysis: Evaporate on a steam bath a portion of *Sample stock solution* from the *Assay*, equivalent to 500 mg of aminophylline, to about one-half its volume. Adjust with 1 N sodium hydroxide to a pH of 7.0, chill, and filter the crystals of theophylline. Retain the filtrate, free from washings. Wash the crystals of theophylline with small portions of ice-cold water, and dry at 105° for 1 h.

Acceptance criteria: The recrystallized theophylline melts at 270°–274°.

• **B.**

Analysis: Transfer 10 mg of the dried precipitate from *Identification* test *A* to a porcelain dish, and add 1 mL of hydrochloric acid and 100 mg of potassium chlorate. Evaporate on a steam bath to dryness, and invert the dish over a vessel containing a few drops of 6 N ammonium hydroxide.

Acceptance criteria: The residue acquires a purple color, which is destroyed by solutions of fixed alkalies.

• **C.**

Analysis: To the filtrate obtained in *Identification* test *A* add 0.5 mL of benzenesulfonyl chloride and 5 mL of 1 N sodium hydroxide to render alkaline, shake by mechanical means for 10 min, and add 5 mL of 3 N hydrochloric acid to acidify. Chill, collect the precipitated disulfonamide of ethylenediamine, and wash with water. Recrystallize the washed precipitate from water, and dry at 105° for 1 h.

Acceptance criteria: The dried precipitate melts at 164°–171°.

ASSAY

• **Procedure**

Sample stock solution: Transfer NLT 5 Suppositories to a tared small dish and a glass rod, and heat on a steam bath until the suppositories are melted. Mix the melt by stirring it with the rod, and cool while stirring. Transfer a portion of the cooled melt, equivalent to 1 g of aminophylline, into a beaker, add 60 mL of hot water and 3 mL of nitric acid, and heat on a steam bath for 15 min with frequent stirring. Cool, transfer to a separator with the aid of 40 mL of ether, shake well, and allow to separate, using a few mL of alcohol if necessary to bring about separation of any emulsion that has formed. Draw the water layer into a 100-mL volumetric flask; wash the ether with two 15-mL portions of water, adding the washings to the volumetric flask; and dilute with water to volume.

Sample solution: Transfer a portion of the *Sample stock solution*, equivalent to 250 mg of aminophylline, to a 250-mL conical flask. Add 10 mL of 6 N ammonium hydroxide and 20 mL of 0.1 N silver nitrate VS, and heat on a steam bath for 15 min. Cool to between 5° and 10° for 20 min; filter, preferably through a filtering crucible of fine porosity under reduced pressure; and wash the precipitate with small portions of water until the last washing gives NMT a faint opalescence with hydrochloric acid. Dissolve the precipitate by pouring over it small volumes of warm 2 N nitric acid, collecting the solution in a conical flask. Wash the filtering crucible a few times with warm water acidified with nitric acid, receiving the washings in the same flask. Cool, and add 2 mL of ferric ammonium sulfate TS.

Analysis: Titrate with 0.1 N ammonium thiocyanate VS. Each mL of 0.1 N ammonium thiocyanate is equivalent to 18.02 mg of theophylline ($C_7H_8N_4O_2$).

Acceptance criteria: 90.0%–110.0%

OTHER COMPONENTS

• **Content of Ethylenediamine**

Sample solution: Weigh a portion of the stirred, congealed mass of the Suppositories from the *Assay*, equivalent to 500 mg of aminophylline, and place in a 500-mL conical flask. Add 150 mL of a mixture of equal volumes of alcohol and ether, and warm gently under reflux for 30 min, with occasional swirling. Cool to room temperature.

Titrimetric system

Mode: Direct titration

Titrant: 0.1 N hydrochloric acid VS

Endpoint detection: Potentiometric

Analysis: Titrate the *Sample solution* using a glass-modified calomel electrode system (replace the saturated potassium chloride solution of the calomel electrode with methanol saturated with lithium chloride). Each mL of 0.1 N hydrochloric acid is equivalent to 3.005 mg of

ethylenediamine ($C_2H_8N_2$).

Acceptance criteria: 152–190 mg of ethylenediamine ($C_2H_8N_2$) per g of theophylline ($C_7H_8N_4O_2$) found in the *Assay*

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers, in a cold place.
- **Labeling:** Label the Suppositories to state the content of anhydrous theophylline.

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

Topic/Question	Contact	Expert Committee
AMINOPHYLLINE SUPPOSITORIES	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:
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