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Erythromycin Ethylsuccinate Tablets

DEFINITION

Erythromycin Ethylsuccinate Tablets contain the equivalent of NLT 90.0% and NMT 120.0% of the labeled amount of erythromycin ($C_{37}H_{67}NO_{13}$).

IDENTIFICATION

• **A. Thin-Layer Chromatography**

Standard solution: 3 mg/mL of USP Erythromycin Ethylsuccinate RS in methanol

Sample solution: Nominally 2.5 mg/mL of erythromycin from powdered Tablets in methanol. Shake this mixture by mechanical means for about 30 min. Centrifuge a portion of this mixture, and use the clear supernatant as the *Sample solution*.

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: Methanol and chloroform (85:15)

Spray reagent: Dehydrated alcohol, *p*-methoxybenzaldehyde, and sulfuric acid (90:5:5)

Analysis

Samples: *Standard solution* and *Sample solution*

Place the plate in an unlined chromatographic chamber, and develop in the *Developing solvent system* until the solvent front has moved about 9 cm. Remove the plate from the chamber, mark the solvent front, and allow the solvent to evaporate. Spray the plate with the *Spray reagent*. Heat it at 100° for 10 min, and examine the chromatograms. The erythromycin and succinic acid moieties appear as black-to-purple spots.

Acceptance criteria: The R_F values of the principal spots from the *Sample solution* correspond to those from the *Standard solution*.

ASSAY

• **Procedure**

(See *Antibiotics—Microbial Assays ⟨81⟩*.)

Test dilution: Blend NLT 4 Tablets for 4 ± 1 min in a high-speed glass blender jar with a sufficient volume of methanol to give a stock solution containing nominally NMT 5 mg/mL of erythromycin. Dilute this stock solution quantitatively with *Buffer B.3* to obtain a *Test dilution* having a concentration assumed to be equal to the median dose level of the standard.

Analysis: Proceed as directed in the chapter.

Acceptance criteria: 90.0%–120.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

FOR NONCHEWABLE TABLETS

Medium: 0.01 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Solution A: 25 mg/mL of ferric chloride

Solution B: Slowly, and with constant mechanical stirring, add 325 mL of sulfuric acid to 173 mL of cold water. Allow the solution to cool, add 2 mL of *Solution A* and 1 g of *p*-dimethylaminobenzaldehyde, and stir to dissolve. Store in a low-actinic flask. Prepare *Solution B* on the day of use.

Standard solution: 0.44 mg/mL of USP Erythromycin RS in *Medium*. Sonicate as necessary to dissolve. Use the *Standard solution* within 5.5 h.

Sample solution: Pass a portion of the solution under test through a filter having a pore size of 0.5 µm or less, discarding the first 5 mL of the filtrate.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: Vis

Analytical wavelength: 480 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

To three separate 50-mL glass-stoppered conical flasks add 2.0 mL of *Standard solution*, 2.0 mL of *Sample solution*, and 2.0 mL of the *Blank*. Place the flasks in an ice bath for about 15 min. At precise 1-min intervals add 10.0 mL of *Solution B* to the *Standard solution*, the *Sample solution*, and the *Blank*, in turn. Immediately after adding *Solution B*, remove each flask from the ice bath, insert the stopper, mix, and allow to stand at room temperature for exactly 30 min. Sequentially determine the absorbance at 480 nm of the *Standard solution* and the *Sample solution* at precise 1-min intervals using the *Blank* to set the spectrophotometer to zero.

Calculate the percentage of the labeled amount of erythromycin ($C_{37}H_{67}NO_{13}$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times P \times F \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

P = potency of erythromycin in USP Erythromycin RS (µg/mg)

F = conversion factor, 0.001 mg/µg

L = label claim (mg/Tablet)

Acceptance criteria: NLT 75% (*Q*) of the labeled amount of erythromycin ($C_{37}H_{67}NO_{13}$) is dissolved.

FOR TABLETS LABELED AS CHEWABLE

Medium: 0.1 M acetate buffer, pH 5.0; 900 mL

Apparatus 2: 75 rpm

Time: 60 min

Buffer A: 33.25 g/L of sodium acetate in water. Adjust with glacial acetic acid to a pH of 4.8 ± 0.1 before diluting to final volume.

Buffer B: pH 7.6 phosphate buffer (see *Reagents, Indicators, and Solutions—Solutions*)

Standard stock solution: 0.5 mg/mL of USP Erythromycin RS in *Buffer A*

Standard solutions: Transfer 8.0-, 4.0-, and 1.0-mL volumes of the *Standard stock solution* to separate 100-mL volumetric flasks, add 6.0 mL of *Buffer B* and 6.0 mL of *Medium* to each flask, and dilute with *Buffer A* to volume. The *Standard solutions* have known concentrations of about 40, 20, and 5 µg/mL of USP Erythromycin RS, respectively.

Sample solution: Transfer 6.0 mL of the solution under test to a 50-mL volumetric flask, add 6.0 mL of *Buffer B*, and heat in boiling water for 30 min. Cool to room temperature, and dilute with *Buffer A* to volume.

Arsenomolybdate stock solution: Dissolve 100 g of ammonium molybdate in 1.7 L of water in a 2-L volumetric flask. Slowly add, with mixing, 84 mL of sulfuric acid. Add 12 g of sodium arsenate dissolved in 100 mL of water. Dilute with water to volume. Store in an amber bottle for 24 h before using. This solution should not come in contact with rubber.

Arsenomolybdate solution: Water and *Arsenomolybdate stock solution* (2:1). Prepare freshly on the day of use.

4.5 M sulfuric acid: Add 1.5 L of water to a 2-L volumetric flask, and place the flask in an ice bath. Slowly add, with stirring, 300 mL of sulfuric acid. Allow the solution to cool, dilute with water to volume, and mix. At the time of use, add 0.5 g of sodium dodecyl sulfate to each L.

Apparatus: To determine the absorbance values, use an automated analyzer consisting of a liquid sampler; a proportioning pump; a manifold; and a spectrophotometer equipped with matched flow cells, suitable recording devices, and analysis capability at 660 nm. See *Figure 1*.

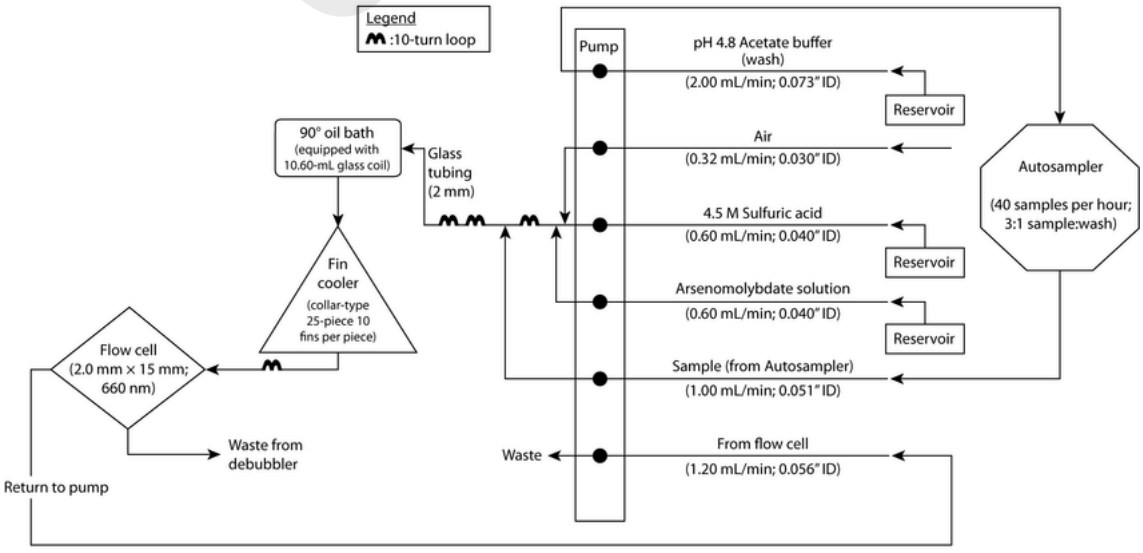

Figure 1

Analysis

Samples: *Standard solutions* and *Sample solution*

Adjust the system until a steady baseline is achieved. Start the sampler, and conduct determinations at a rate of about 40–60/h with a 3:1 (sample/wash) ratio. Adjust the analyzer flow rates, if necessary, to optimize system performance.

Calculate the percentage of the labeled amount of erythromycin ($C_{37}H_{67}NO_{13}$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times P \times F \times (1/L) \times 100$$

A_U = response of the *Sample solution*

A_S = response of the *Standard solution*

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

V = volume of *Medium*, 900 mL

P = potency of erythromycin in USP Erythromycin RS (µg/mg)

F = conversion factor, 0.001 mg/µg

L = label claim (mg/Tablet)

Acceptance criteria: NLT 75% (Q) of the labeled amount of erythromycin ($C_{37}H_{67}NO_{13}$) is dissolved.

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

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry 100 mg in vacuum at a pressure not exceeding 5 mm of mercury at 60° for 3 h.

Acceptance criteria: NMT 4.0%; Chewable Tablets are exempt from this requirement.

• **Water Determination, *Method I*⟨921⟩:** NMT 5.0%; Chewable Tablets only

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers,protect from light and moisture, and store at a temperature below 30°.

• **Labeling:** Label the Chewable Tablets to indicate that they are to be chewed before swallowing.

• **USP Reference Standards ⟨11⟩**

USP Erythromycin RS

USP Erythromycin Ethylsuccinate RS

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

Topic/Question	Contact	Expert Committee
ERYTHROMYCIN ETHYLSUCCINATE TABLETS	Julie Zhang Associate Science & Standards Liaison	BIO42020 Biologics Monographs 4 - Antibiotics
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	BIO42020 Biologics Monographs 4 - Antibiotics

Chromatographic Database Information: Chromatographic Database

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