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Estropipate Tablets

» Estropipate Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of estropipate ($C_{18}H_{22}O_5S \cdot C_4H_{10}N_2$).

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—

USP Estropipate RS

Identification—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: 0.05 M pH 6.8 phosphate buffer; 900 mL.

Apparatus 2: 75 rpm.

Time: 30 minutes.

Determine the amount of $C_{18}H_{22}O_5S \cdot C_4H_{10}N_2$ dissolved by employing the following method.

Diluent and *Mobile phase*—Proceed as directed in the *Assay*.

System suitability solution—Transfer about 100 mg of 4'-nitroacetophenone, accurately weighed, to a 100-mL volumetric flask, and dissolve in methanol, sonicating if necessary. Dilute with methanol to volume, and mix. Pipet 2 mL of this solution into a 250-mL volumetric flask, dilute with water to volume, and mix.

Standard solution—Dissolve an accurately weighed quantity of USP Estropipate RS in *Diluent*, sonicating if necessary, and dilute quantitatively with *Diluent* to obtain a solution having a known concentration of about 1 mg per mL. Pipet 2 mL of this solution into a 100-mL volumetric flask, dilute with water to volume, and mix. Pipet 4 mL of the solution so obtained into a second 100-mL volumetric flask, add 8.0 mL of the *System suitability solution*, dilute with water to volume, and mix.

Test solution—Transfer an accurately measured volume of a filtered portion of the solution under test, equivalent to about 20 µg of estropipate, to a 25-mL volumetric flask. Dilute with water to volume if the contents are less than the nominal volume of the flask, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—Prepare as directed in the *Assay*. To evaluate the system suitability requirements, use the *Standard solution*.

Procedure—Separately inject equal volumes (about 300 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity of $C_{18}H_{22}O_5S \cdot C_4H_{10}N_2$ dissolved.

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{18}H_{22}O_5S \cdot C_4H_{10}N_2$ is dissolved in 30 minutes.

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

Procedure for content uniformity—

Diluent, *Mobile phase*, *System suitability solution*, *Standard preparation*, and *Chromatographic system*—Prepare as directed in the *Assay*.

Test preparation—Transfer 1 Tablet to a 50-mL volumetric flask, add 20 mL of water, insert the stopper, and shake by mechanical means for about 30 minutes or until the Tablet disintegrates. Add 20 mL of methanol, insert the stopper, and shake by mechanical means for about 60 minutes. Dilute with *Diluent* to volume, and mix. Transfer an accurately measured volume of this stock solution, equivalent to about 0.25 mg of estropipate, to a 25-mL volumetric flask, dilute with *Diluent* to volume, and mix. Pass this solution through a solvent-resistant membrane filter having a 1-µm or finer porosity, discarding the first portion of the filtrate.

Procedure—Proceed as directed in the *Assay*, except to use the *Test preparation* instead of the *Assay preparation*.

Assay—

Diluent—Prepare a mixture of methanol and water (1:1).

Mobile phase—Dissolve 13.6 g of monobasic potassium phosphate in 1000 mL of water, and mix. Mix 600 mL of the resulting solution with 200 mL of methanol, add 200 mL of acetonitrile with stirring, and mix. Filter, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Estropipate RS in *Diluent*, sonicating if necessary, and dilute quantitatively with *Diluent* to obtain a solution having a known concentration of about 1 mg per mL. Pipet 1.0 mL of this solution into a 100-mL volumetric flask, dilute with *Diluent* to volume, and mix.

System suitability solution—Transfer about 100 mg of 4'-nitroacetophenone, accurately weighed, to a 100-mL volumetric flask, and dissolve in methanol, sonicating if necessary. Dilute with methanol to volume, and mix. Pipet 5 mL of this solution into a 200-mL volumetric flask, dilute with *Diluent* to volume, and mix. Pipet 5 mL of the solution so obtained into a 25-mL volumetric flask, dilute with *Standard preparation* to volume, and mix.

Assay preparation—Transfer 20 Tablets to a 1000-mL volumetric flask, add 200 mL of water, insert the stopper, and shake by mechanical means for about 30 minutes or until the Tablets disintegrate completely. Add 200 mL of methanol, insert the stopper, and shake by mechanical means for about 60 minutes. Dilute with *Diluent* to volume, and mix. Transfer an accurately measured volume of this stock solution, equivalent to about 0.25 mg of estropipate, to a 25-mL volumetric flask, dilute with *Diluent* to volume, and mix. Pass this solution through a solvent-resistant membrane filter having a 1-µm or finer porosity, discarding the first portion of the filtrate.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 213-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.85 for 4'-nitroacetophenone and 1.0 for estropipate; the resolution, *R*, between estropipate and 4'-nitroacetophenone is not less than 3.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of estropipate ($C_{18}H_{22}O_5S \cdot C_4H_{10}N_2$) in each Tablet taken by the formula:

$$(25C/V)(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Estropipate RS in the *Standard preparation; V* is the volume, in mL, of the stock solution taken to prepare the *Assay preparation;* and r_U and r_S are the peak responses for estropipate 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
ESTROPIPATE TABLETS	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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