Status: Currently Official on 14-Feb-2025
Official Date: Official Prior to 2013
Document Type: USP Monographs
DocId: GUID-6CAA67A5-8D03-47FA-9CD5-96148E7555BC_2_en-US
DOI: https://doi.org/10.31003/USPNF_M30650_02_01
DOI Ref: 8cs4e

Estradiol Tablets

» Estradiol Tablets contain not less than 90.0 percent and not more than 115.0 percent of the labeled amount of $C_{18}H_{24}O_2$.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩—

USP Estradiol RS
USP Estrone RS

Identification—Place a quantity of finely powdered Tablets, equivalent to about 4 mg of estradiol, in a screw-capped, 20-mL vial. Add 10 mL of chloroform, and sonicate for 2 minutes. Filter through medium-porosity filter paper. Apply 20 µL each of this solution and a Standard solution of USP Estradiol RS in chloroform containing 0.4 mg per mL to a suitable thin-layer chromatographic plate (see *Chromatography ⟨621⟩*) coated with a 0.25-mm layer of chromatographic silica gel mixture. Allow the spots to dry, and develop the chromatogram in a lined chamber with a solvent system consisting of a mixture of toluene and acetone (4:1) until the solvent front has moved 10 cm beyond the starting line. Remove the plate from the developing chamber, mark the solvent front, and allow to air-dry. Spray the plate with a mixture of methanol and sulfuric acid (1:1), and heat at 100° for about 5 minutes: the principal spots obtained from the test solution and the Standard solution have the same color and R_F value.

Dissolution ⟨711⟩—

Medium: 0.3% sodium lauryl sulfate in water; 500 mL.
Apparatus 2: 100 rpm.
Time: 60 minutes.
Mobile phase—Prepare a suitable degassed and filtered solution of water and acetonitrile (55:45).
Standard solution—Prepare a solution of USP Estradiol RS in methanol having an accurately known concentration of about 0.02 mg per mL. Dilute aliquots of this solution with *Medium* to obtain a final solution having a concentration approximately equal to the expected concentration of drug in the *Medium*, assuming 100% dissolution.
Test solution—Use a filtered portion of the solution under test from the dissolution vessel.
Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 205-nm detector and a 4.6-mm × 7.5-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph replicate injections of the *Standard preparation,* and record the peak areas as directed for *Procedure:* the tailing factor is not more than 2.0; and the relative standard deviation is not more than 2.0%.
Procedure—Separately inject equal volumes (about 100 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity of $C_{18}H_{24}O_2$ dissolved by comparison of the peak areas obtained from the *Test solution* and the *Standard solution*.
Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_{18}H_{24}O_2$ is dissolved in 60 minutes.

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

Chromatographic purity—

Solution A—Prepare a degassed mixture of water and acetonitrile (8:2).
Solution B—Prepare a degassed mixture of acetonitrile and water (8:2).
Diluent—Prepare a mixture of water and acetonitrile (6:4).
Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system.* Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).
System suitability solution—Dissolve accurately weighed quantities of USP Estradiol RS and USP Estrone RS in acetonitrile to obtain a solution having concentrations of 0.5 mg per mL and 0.3 mg per mL, respectively. Pipet 2 mL of this solution into a 50-mL volumetric flask, and dilute with *Diluent* to volume.
Test solution—Transfer a number of Tablets, containing a combined amount of 4 to 8 mg of estradiol based on the label claim, to a suitable flask, add a volume of *Diluent* equivalent to about 5 mL per each mg of estradiol, swirl until the Tablets are completely disintegrated, then

shake for 15 minutes, and allow the solids to settle. Pass a portion of this solution through a 0.45-µm PVDF filter, discarding the first 2 mL of the filtrate. This solution contains about 0.2 mg of estradiol per mL.

Chromatographic system (see Chromatography ⟨621⟩)—The liquid chromatograph is equipped with a 200-nm detector and a 4.0-mm × 12.5-cm column that contains 5-µm packing L7. The flow rate is about 1 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0–5	100→90	0→10	linear gradient
5–15	90→50	10→50	linear gradient
15–25	50→0	50→100	linear gradient
25–35	0	100	isocratic
35–35.1	0→100	100→0	linear gradient
35.1–40	100	0	re-equilibration

Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure.* Identify the components based on their relative retention times which are 1.0 for estradiol and about 1.1 for estrone: the resolution, *R,* between estradiol and estrone is not less than 3.0; the tailing factors for estradiol and estrone peaks are not more than 1.5; and the relative standard deviation for replicate injections is not more than 2% for each peak.

Procedure—Inject a volume (about 10 µL) of the *Test solution* into the chromatograph, record the chromatogram, and measure the peak responses. Calculate the percentage of each impurity in the portion of Tablets taken by the formula:

$$100(r_i/r_s)$$

in which r_i is the peak response for each impurity; and r_s is the sum of the responses of all the peaks: not more than 5% of total impurities is found. Disregard any peaks observed in the blank.

Assay—

Mobile phase, Internal standard solution, Standard preparation, and *Chromatographic system*—Proceed as directed in the Assay under Estradiol.

Assay preparation—Weigh and finely powder not fewer than 10 Tablets. Transfer a portion of the powder, equivalent to about 8 mg of estradiol, to a 100-mL volumetric flask. Add 4 mL of water, and swirl. Add 10.0 mL of *Internal standard solution* and about 60 mL of methanol. Shake by mechanical means for 15 minutes, dilute with methanol to volume, mix, and allow the solids to settle. Filter a portion, discarding the first 10 mL of the filtrate. Mix 5.0 mL of the subsequent filtrate with 5.0 mL of methanol and 10.0 mL of water.

Procedure—Proceed as directed for *Procedure* in the Assay under Estradiol. Calculate the quantity, in mg, of $C_{18}H_{24}O_2$ in the portion of Tablets taken by the formula:

$$0.4C(R_U/R_S)$$

in which the terms are as defined therein.

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

Topic/Question	Contact	Expert Committee
ESTRADIOL TABLETS	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 34(3)

Current DocID: GUID-6CAA67A5-8D03-47FA-9CD5-96148E7555BC_2_en-US

Previous DocID: GUID-6CAA67A5-8D03-47FA-9CD5-96148E7555BC_1_en-US
DOI: https://doi.org/10.31003/USPNF_M30650_02_01
DOI ref: 8cs4e