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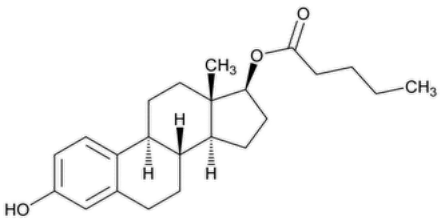
Estradiol Valerate



$C_{23}H_{32}O_3$ 356.50

Estra-1,3,5(10)-triene-3,17-diol(17β)-, 17-pentanoate;

Estradiol 17-valerate CAS RN®: 979-32-8; UNII: OKG364O896.

DEFINITION

Estradiol Valerate contains NLT 98.0% and NMT 102.0% of estradiol valerate ($C_{23}H_{32}O_3$).

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

- **Procedure**

Solution A: Water

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	48	52
1	48	52
10	35	65
17.5	0	100
26	0	100

Standard solution: 1.2 mg/mL of USP Estradiol Valerate RS in acetonitrile

Sample solution: 1.2 mg/mL of Estradiol Valerate in acetonitrile

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 10-cm; 2.6-µm packing ▲L87▲ (USP 1-Aug-2021)

Flow rate: 2.0 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of estradiol valerate ($C_{23}H_{32}O_3$) in the portion of Estradiol Valerate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of estradiol valerate from the *Sample solution*

r_S = peak response of estradiol valerate from the *Standard solution*

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

C_U = concentration of Estradiol Valerate in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0%

IMPURITIES

Change to read:

• **Organic Impurities**

Solution A, Solution B, Mobile phase, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 1.25 mg/mL of USP Estradiol Valerate Identification Mixture RS in acetonitrile

Standard solution: 5 µg/mL of USP Estradiol Valerate RS in acetonitrile

Sample solution: ▲5000 µg/mL▲ (USP 1-Aug-2021) of Estradiol Valerate in acetonitrile

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 2.5 between estradiol-9-ene valerate and estradiol valerate, *System suitability solution*

Relative standard deviation: NMT 10.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Estradiol Valerate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of estradiol valerate from the *Standard solution*

C_S = concentration of USP Estradiol Valerate RS in the *Standard solution* ▲(µg/mL)▲ (USP 1-Aug-2021)

C_U = concentration of Estradiol Valerate in the *Sample solution* ▲(µg/mL)▲ (USP 1-Aug-2021)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. ▲The reporting threshold is▲ (USP 1-Aug-2021) 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Estradiol	0.1	1.0	0.5
Estradiol-9-ene valerate	0.9	2.0	0.5
Estradiol valerate	1.0	—	—
4-Methylestradiol valerate	1.3	1.0	0.5

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Estradiol divalerate	1.7	1.0	0.15
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

• **Free Acid**

Diluent: Neutralize 25 mL of alcohol, in a conical flask, with 0.01 N sodium hydroxide VS to a faint blue color, using bromothymol blue TS.

Sample solution: 500 mg of Estradiol Valerate in 25 mL of *Diluent*

Analysis: Rapidly titrate the *Sample solution* with 0.01 N sodium hydroxide VS to a faint blue color. Each milliliter of 0.01 N sodium hydroxide is equivalent to 1.021 mg of valeric acid.

Acceptance criteria: NMT 0.5%, as valeric acid

SPECIFIC TESTS

• **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

Sample solution: 25 mg/mL, uncorrected for moisture, in methanol

Acceptance criteria: +41° to +47

• **Water Determination** ⟨921⟩, *Method I*: NMT 0.1%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Estradiol Valerate RS

USP Estradiol Valerate Identification Mixture RS

Contains a mixture of the following 5 compounds:

Estradiol valerate.
Estradiol;
Estra-1,3,5(10)-triene-3,17β-diol.
$C_{18}H_{24}O_2$ 272.38

Estradiol-9-ene valerate;
3-Hydroxyestra-1,3,5(10),9(11)-tetraen-17β-yl valerate. $C_{23}H_{30}O_3$ 354.48

4-Methylestradiol valerate;
3-Hydroxy-4-methylestra-1,3,5(10)-trien-17β-yl valerate. $C_{24}H_{34}O_3$ 370.52

Estradiol divalerate;
Estra-1,3,5(10)-trien-3,17β-diyl divalerate. $C_{28}H_{40}O_4$ 440.61

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

Topic/Question	Contact	Expert Committee
ESTRADIOL VALERATE	Documentary Standards Support Associate Scientific Liaison.	NBDS2020 Non-botanical Dietary Supplements

Chromatographic Database Information: Chromatographic Database

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