Edition: BP 2025 (Ph. Eur. 11.6 update)

Estriol Cream

General Notices

Action and use

Estrogen.

DEFINITION

Estriol Cream contains Estriol in a suitable basis.

The cream complies with the requirements stated under Topical Semi-solid Preparations and with the following requirements.

Content of estriol, $C_{18}H_{24}O_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions in *methanol*.
(1) To a quantity of cream containing 2 mg of Estriol add 50 mL of solvent, heat on a water bath and mix until the cream has completely dispersed, cool the contents in ice, centrifuge and use the supernatant liquid.
(2) 0.004% w/v of *estriol BPCRS*.
(3) 0.004% w/v each of *estriol BPCRS* and *prednisolone BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a silica gel 60 high performance precoated plate (Merck HPTLC silica gel 60 is suitable).
(b) Use the mobile phase as described below.
(c) Apply 5 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry the plate in a horizontal position at 100 to 105°. Dilute 2 mL of *sulfuric acid* to 100 mL with *ethanol (96%)* and spray the solution evenly onto the plate. Examine the plate in daylight.

MOBILE PHASE

10 volumes of *methanol* and 90 volumes of *dichloromethane*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) shows two clearly separated spots.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) is similar in position, colour and size to that in the chromatogram obtained with solution (2).

B. In the Assay, the chromatogram obtained with solution (1) shows a peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).

TESTS

Acidity

pH, 3.5 to 4.5, Appendix V L.

Disperse 10 g of the cream in 10 mL of *water*, with continuous stirring throughout the pH determination.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in *methanol*.

(1) To a quantity of cream containing 0.5 mg of Estriol add 20 mL of solvent, heat on a water bath and mix until the cream has completely dissolved, allow to cool to room temperature and add sufficient solvent to produce 25 mL. Cool the contents in ice for 15 minutes, centrifuge and use the supernatant liquid.
(2) Dilute 5 volumes of solution (1) to 100 volumes, further dilute 10 volumes of this solution to 100 volumes.
(3) Dilute 10 volumes of solution (2) to 100 volumes.
(4) 0.01% w/v of *estriol impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Nucleosil C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 35°.
(e) Use a detection wavelength of 280 nm.
(f) Inject 100 µL of each solution.

MOBILE PHASE

5 volumes of *methanol*, 38 volumes of *acetonitrile* and 57 volumes of *water*.

For solutions (3) and (4), when the chromatograms are recorded under the prescribed conditions, the retention times for estriol and 16-epi-estriol are about 5 minutes and about 7 minutes respectively.

SYSTEM SUITABILITY

The test is not valid unless, (a) in the chromatogram obtained with solution (4), the *resolution factor* between the peaks due to estriol and 16-epi-estriol is at least 2.5 and (b) in the chromatogram obtained with solution (3) the *signal-to-noise ratio* of the principal peak is at least 10.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the sum of the areas of any *secondary peaks* is not greater than twice the principal peak in the chromatogram obtained with solution (2) (1%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (3) (0.05%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in *methanol*.

(1) To a quantity of cream containing 0.5 mg of Estriol add 20 mL of *methanol*, heat on a water bath and mix until the cream has completely dispersed, allow to cool to room temperature and add sufficient *methanol* to produce 25 mL, transfer to a centrifuge tube and cool the contents in ice for 15 minutes, centrifuge and dilute 5 volumes of the supernatant liquid to 100 volumes with *methanol*.
(2) 0.0001% w/v of *estriol BPCRS*.
(3) 0.01% w/v of *estriol impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic procedure described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the peaks due to estriol and 16-epi-estriol is at least 2.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{18}H_{24}O_3$ in the cream using the declared content of $C_{18}H_{24}O_3$ in *estriol BPCRS*.