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

Glyceryl Trinitrate Transdermal Patches

General Notices

DEFINITION

Glyceryl Trinitrate Transdermal Patches contain glyceryl trinitrate in a suitable matrix or reservoir presentation. They are prepared from Glyceryl Trinitrate Solution.

PRODUCTION

A suitable dissolution test is carried out to demonstrate the appropriate release of glyceryl trinitrate.

The transdermal patches comply with the requirements stated under Transdermal Patches and with the following requirements.

Content of glyceryl trinitrate, $C_3H_5N_3O_9$

90.0 to 115.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Clean the outer surface of a patch using a lint-free cloth moistened with *methanol*. Remove the release liner and score the exposed surface. Place the patch in a flask containing sufficient *methanol* to produce a solution containing 0.1% w/v of glyceryl trinitrate, mix with the aid of ultrasound in a water bath at 40° for 15 minutes and then shake mechanically at room temperature for 3 hours. Dilute the methanolic extract with sufficient *water* to produce a final concentration of 0.05% w/v of glyceryl trinitrate.
(2) Dilute a quantity of *glyceryl trinitrate solution BPCRS* with *methanol (50%)* to produce a solution containing 0.05% w/v of glyceryl trinitrate.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel* (Merck silica gel plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air, spray with freshly prepared *potassium iodide and starch solution*. Expose the plate to *ultraviolet light (254 nm)* for 15 minutes and examine in daylight.

MOBILE PHASE

20 volumes of *ethyl acetate* and 80 volumes of *toluene*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position and colour to that in the chromatogram obtained with solution (2).

B. In the test for Uniformity of content, 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

Related substances

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

(1) Clean the outer surface of five patches using a lint-free cloth moistened with *methanol*. Remove the release liners and score the exposed surfaces. Place the patches in a flask containing sufficient *methanol* to produce a solution containing 0.1% w/v of glyceryl trinitrate, mix with the aid of ultrasound in a water bath at 40° for 15 minutes and then shake mechanically at room temperature for 3 hours. Dilute the methanolic extract with sufficient *water* to produce a final concentration of 0.05% w/v of glyceryl trinitrate.
(2) Dilute 1 volume of solution (1) to 100 volumes with *methanol (50%)*.
(3) Dilute a quantity of *glyceryl trinitrate solution BPCRS* with sufficient 1M *hydrochloric acid* to produce a solution containing 0.05% w/v of glyceryl trinitrate and heat in a reaction vial at 100° for 30 minutes.

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 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 210 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Equal volumes of *acetonitrile* and *water*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) closely resembles the reference chromatogram supplied with *glyceryl trinitrate solution BPCRS* in that it shows a principal peak due to glyceryl trinitrate and two clearly separated peaks due to the dinitrate impurities with retention times relative to glyceryl trinitrate of approximately 0.5.

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) (1%);

the sum of the areas of any *secondary peaks* is not greater than three times the area of the principal peak in the chromatogram obtained with solution (2) (3%).

Disregard any peak with an area less than 0.1 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

Uniformity of content

Comply with the requirements stated under *uniformity of content*, Appendix XII C3, Test C, with respect to the individual content of each dosage unit and using the following method of analysis. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Clean the outer surface of a patch using a lint-free cloth moistened with *methanol*. Remove the release liner and score the exposed surface. Place the patch in a flask containing sufficient *methanol* to produce a solution containing 0.1%

w/v of glyceryl trinitrate, mix with the aid of ultrasound in a water bath at 40° for 15 minutes, shake mechanically at room temperature and dilute a volume of the solution with an equal volume of *water*.
(2) Dilute a quantity of *glyceryl trinitrate solution BPCRS* with sufficient *methanol (50%)* to produce a solution containing 0.05% w/v of glyceryl trinitrate.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

DETERMINATION OF CONTENT

Calculate the content of $C_3H_5N_3O_9$ in the transdermal patch using the declared content of $C_3H_5N_3O_9$ in *glyceryl trinitrate solution BPCRS*.

ASSAY

Use the average of the 10 results obtained in the test for Uniformity of content.

IMPURITIES

A. Glyceryl-1,2-dinitrate,
B. Glyceryl-1,3-dinitrate.