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

Glyceryl Trinitrate Ointment

General Notices

Action and use

Vasodilator.

DEFINITION

Glyceryl Trinitrate Ointment contains Glyceryl Trinitrate in a suitable basis.

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

Content of glyceryl trinitrate, $C_3H_5N_3O_9$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) To a quantity of the ointment containing 40 mg of Glyceryl Trinitrate add 80 mL of *methanol*, disperse with the aid of ultrasound for 30 minutes, cool in ice and filter. Dilute 1 volume of the filtrate to 5 volumes with *methanol*.
(2) Dilute a quantity of *glyceryl trinitrate solution BPCRS* with sufficient *methanol* to produce a solution containing approximately 0.01% w/v of Glyceryl Trinitrate.
(3) Equal volumes of solutions (1) and (2).

CHROMATOGRAPHIC CONDITIONS

(a) Use a *silica gel plate* (Merck silica gel 60 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 a current of cool 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*.

SYSTEM SUITABILITY

The principal spot in the chromatogram obtained with solution (3) appears as a single compact spot.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds 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

Related substances

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

(1) To a quantity of the ointment containing 50 mg of Glyceryl Trinitrate add 70 mL of *methanol* and completely disperse with the aid of ultrasound. Cool the contents in ice for 30 minutes, allow to attain room temperature, add sufficient *methanol* to produce 100 mL and centrifuge.
(2) Dilute 1 volume of solution (1) to 100 volumes with *methanol*.
(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 (production of the dinitrate impurities).
(4) Dilute 1 volume of solution (2) to 10 volumes with *methanol*.

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 an ambient column temperature.
(e) Use a detection wavelength of 210 nm.
(f) Inject 50 µL of each solution.
(g) For solution (1), allow the chromatography to proceed for three times the retention time of the principal peak.

MOBILE PHASE

50 volumes of *acetonitrile R1* and 50 volumes of *water*.

When the chromatograms are recorded under the prescribed conditions the retention times relative to glyceryl trinitrate (retention time, about 11 minutes) are: glyceryl mononitrate, about 0.23; 1,3-glyceryl dinitrate, about 0.42; 1,2-glyceryl dinitrate, about 0.45.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) 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.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak due to glyceryl mononitrate, 1,3-glyceryl dinitrate or 1,2-glyceryl dinitrate 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 other *secondary peaks* is not greater than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

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

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

ASSAY

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

(1) To a quantity of the ointment containing 40 mg of Glyceryl Trinitrate add 70 mL of *methanol* and, completely disperse with the aid of ultrasound. Cool the contents in ice for 30 minutes, allow to attain room temperature, add sufficient *methanol* to produce 100 mL and centrifuge.
(2) Dilute a quantity of *glyceryl trinitrate solution BPCRS* with sufficient *methanol* to produce a solution containing 0.04% w/v of Glyceryl Trinitrate.
(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 1.3 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 225 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

50 volumes of *methanol* and 50 volumes of *water*.

When the chromatograms are recorded under the prescribed conditions the retention times relative to glyceryl trinitrate (retention time, about 9 minutes) are: 1,3-glyceryl dinitrate, about 0.4; 1,2-glyceryl dinitrate, about 0.45; isosorbide dinitrate, about 0.7.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the peak to valley ratio between 1,3-glyceryl dinitrate and 1,2-glyceryl dinitrate is at least 5.

DETERMINATION OF CONTENT

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