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

Glyceryl Trinitrate Tablets

General Notices

Glyceryl Trinitrate Sublingual Tablets; Trinitrin Tablets; Nitroglycerin Tablets

DEFINITION

Glyceryl Trinitrate Tablets are *sublingual tablets* made with Mannitol as the basis and may be prepared by adding Glyceryl Trinitrate Solution of an appropriate concentration to dried granules of Mannitol, mixing intimately, drying at a temperature not exceeding 50° or without heating for not more than 4 hours and compressing.

CAUTION Undiluted glyceryl trinitrate can be exploded by percussion or excessive heat. Appropriate precautions should be exercised and only exceedingly small amounts should be isolated.

The tablets comply with the requirements stated under Oromucosal Preparations and with the following requirements.

Content of glyceryl trinitrate, $C_3H_5N_3O_9$

85.0 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) Extract a quantity of the powdered tablets containing 0.5 mg of glyceryl trinitrate with 1 mL of *acetone* and centrifuge.
(2) Dilute a quantity of *glyceryl trinitrate solution BPCRS* with sufficient *water* to produce a solution containing 0.05% w/v of glyceryl trinitrate.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel G*.
(b) Use the mobile phase as described below.
(c) Apply 20 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in a stream of air, spray with *diphenylamine solution R1* and irradiate for 15 minutes with *ultraviolet light (365 nm)*. Examine the plate in daylight.

MOBILE PHASE

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. Extract a quantity of the powdered tablets containing 3 mg of glyceryl trinitrate with 5 mL of *ether* and filter. Evaporate the ether and dissolve the residue in 0.2 mL of *sulfuric acid* containing a trace of *diphenylamine*. An intense blue colour is produced.

TESTS

Related substances

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

(1) Mix a quantity of the powdered tablets containing 2.5 mg of glyceryl trinitrate with 10 mL of *acetonitrile* with the aid of ultrasound, filter through a 4-µm filter and dilute one volume of the filtrate with an equal volume of *water*.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase.
(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 with *octadecylsilyl silica gel for chromatography* (5 µm) (Nucleosil ODS 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 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

40 volumes of *acetonitrile* and 60 volumes of *water*.

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 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 such 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

Tablets containing less than 2 mg and/or less than 2% w/w of glyceryl trinitrate comply with the requirements stated under Tablets using the following method of analysis. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Add 2 mL of *acetonitrile* to one tablet, mix with the aid of ultrasound for 5 minutes, filter through a 4-µm filter and dilute 1 volume of the filtrate with an equal volume of *water*.
(2) Dilute *glyceryl trinitrate solution BPCRS* with the mobile phase to produce a solution containing the equivalent amount of glyceryl trinitrate as that expected for solution (1).
(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

The chromatographic conditions described under Related substances may be used, with the exception of the run time.

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 with retention times relative to glyceryl trinitrate of approximately 0.5.

DETERMINATION OF CONTENT

Calculate the content of $C_3H_5N_3O_9$ in each tablet from the chromatograms obtained and using the declared content of $C_3H_5N_3O_9$ in *glyceryl trinitrate solution BPCRS*.

ASSAY

Use the average of the individual results determined in the test for Uniformity of content.

STORAGE

Glyceryl Trinitrate Tablets should be protected from light and stored in a glass container closed by means of a screw closure lined with aluminium or tin foil; additional packing that absorbs glyceryl trinitrate should be avoided. Glyceryl Trinitrate Tablets should be issued for patients in containers of not more than 100 tablets.