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

Glyceryl Trinitrate Sublingual Spray

General Notices

DEFINITION

Glyceryl Trinitrate Sublingual Spray contains Glyceryl Trinitrate Solution in a suitable vehicle either in a suitable pressurised container or in a container fitted with a spray device.

PRODUCTION

A suitable test is carried out to demonstrate the uniformity of dose.

The oromucosal spray complies with the requirements stated under Oromucosal Preparations and with the following requirements.

Content of glyceryl trinitrate, $C_3H_5N_3O_9$

80.0 to 120.0% of the amount stated to be delivered per metered dose.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using a *TLC silica gel plate* (Merck silica gel plates are suitable) and a mixture of 20 volumes of *ethyl acetate* and 80 volumes of *toluene* as the mobile phase. Apply separately to the plate 5 µL of each of the following solutions. For solution (1) expel a number of metered doses containing the equivalent of about 4 mg of glyceryl trinitrate into a beaker, add 5 mL of *acetone*, transfer to a graduated flask and add sufficient *acetone* to produce 10 mL. For solution (2) dilute a quantity of *glyceryl trinitrate solution BPCRS* with *methanol (50%)* to produce a solution containing 0.04% w/v of glyceryl trinitrate. Solution (3) is a mixture of equal volumes of solutions (1) and (2). After removal of the plate, allow it to dry in air and spray with freshly prepared *potassium iodide and starch solution*. Expose the plate to *ultraviolet light (254 nm)* for 15 minutes and examine in daylight. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2). The principal spot in the chromatogram obtained with solution (3) appears as a single compact spot.
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. For solution (1) expel a number of metered doses containing the equivalent of about 5 mg of glyceryl trinitrate into a beaker, dilute to 5 mL with *methanol*, mix well and add sufficient *water* to produce 10 mL. For solution (2) dilute 1 volume of solution (1) to 100 volumes with *methanol (50%)*. For solution (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.

The chromatographic procedure may be carried out using (a) a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Nucleosil C18 is suitable), (b) as the mobile phase with a flow rate of 1.0 mL per minute a mixture of 50 volumes of *acetonitrile* and 50 volumes of *water* and (c) a detection wavelength of 210 nm.

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.

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%) and the sum of 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%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. For solution (1) collect 10 metered doses in a vessel avoiding loss of material, dissolve the expelled material in *methanol* and dilute with sufficient *methanol* to produce a solution containing the equivalent of 0.04% w/v of glyceryl trinitrate. For solution (2) dilute a quantity of *glyceryl trinitrate solution BPCRS* with sufficient *methanol (50%)* to produce a solution containing 0.04% w/v of glyceryl trinitrate.

The chromatographic procedure may be carried out using (a) a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Nucleosil C18 is suitable), (b) as the mobile phase with a flow rate of 1.3 mL per minute a mixture of 50 volumes of *methanol* and 50 volumes of *water* and (c) a detection wavelength of 225 nm.

Calculate the content of $C_3H_5N_3O_9$ per metered dose using the declared content of $C_3H_5N_3O_9$ in *glyceryl trinitrate solution BPCRS*.