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

Benzoyl Peroxide Gel

General Notices

Action and use

Used topically in the treatment of acne.

DEFINITION

Benzoyl Peroxide Gel is a solution of Hydrous Benzoyl Peroxide in a suitable water-soluble basis.

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

Content of anhydrous benzoyl peroxide, $C_{14}H_{10}O_4$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, protected from light, using the following solutions.
(1) Shake a quantity of the preparation being examined containing the equivalent of 50 mg of anhydrous benzoyl peroxide with 10 mL of *dichloromethane* and filter.
(2) 0.5% w/v of *benzoyl peroxide* in *dichloromethane*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}*.
(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, allow it to dry in air and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

1 volume of *glacial acetic acid*, 2 volumes of *dichloromethane* and 50 volumes of *toluene*.

CONFIRMATION

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

B. In the test for Related substances, the chromatogram obtained with solution (1) shows a peak with the same retention time as the peak due to benzoyl peroxide in the chromatogram obtained with solution (4).

TESTS

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. Prepare a mixture of 0.1 volumes of *acetic acid* and 999.9 volumes of *acetonitrile* (solvent A).

(1) Add 1 mL of solvent A to a quantity of the gel containing the equivalent of 25 mg of anhydrous benzoyl peroxide. Mix using a vortex mixer until a uniform suspension is obtained. Add three 1-mL quantities of *acetonitrile* and mix using a vortex mixer between each addition. Add a further 15 mL of *acetonitrile* and mix with the aid of ultrasound for 3 minutes. Add sufficient *acetonitrile* to produce 100 mL. Dilute 1 volume to 10 volumes with *acetonitrile*.
(2) Dilute 1 volume of solution (1) to 100 volumes with *acetonitrile*.
(3) 0.003% w/v of *benzoic acid*, 0.0003% w/v of *ethyl benzoate* and 0.0003% w/v of *benzaldehyde* in *acetonitrile*.
(4) 0.0025% w/v of *benzoyl peroxide* in *acetonitrile*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped phenyl ethyl silica gel for chromatography* (4 µm) (Phenomenex Synergi Polar RP is suitable) fitted with a suitable stainless steel guard column packed with *octadecylsilyl silica gel for chromatography*.
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.3 mL per minute.
(d) Use a column temperature of 35°.
(e) Use a detection wavelength of 235 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 0.00042% v/v of *orthophosphoric acid*.

Mobile phase B *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-5	65	35	isocratic
5-15	65→15	35→85	linear gradient
15-18	15	85	isocratic
18-20	15→65	85→35	linear gradient
20-31	65	35	re-equilibration

When the chromatograms are recorded under the prescribed conditions the retention times relative to benzoyl peroxide (retention time about 14.5 minutes) are: benzoic acid, about 0.3; benzaldehyde, about 0.5 and ethyl benzoate, about 0.8.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to benzoic acid and benzaldehyde is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

Identify the peaks due to benzoic acid, benzaldehyde and ethyl benzoate using the chromatogram obtained with solution (3) and multiply the areas of these peaks by the corresponding correction factors: benzoic acid, 1.50; benzaldehyde, 1.74; and ethyl benzoate, 1.72.

the area of any peak corresponding to benzoic acid is not greater than 10 times the area of the principal peak in the chromatogram obtained with solution (2) (10%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%).

ASSAY

Mix a quantity of the preparation being examined containing the equivalent of 0.25 g of anhydrous benzoyl peroxide with 50 mL of *acetone* and add sufficient *acetone* to produce 100 mL. To 10 mL add 25 mL of a 20% w/v solution of *potassium iodide*, mix, stopper the flask and allow to stand for 15 minutes protected from light. Add 25 mL of *acetone* and titrate with 0.01M *sodium thiosulfate VS* using *starch mucilage*, added towards the end of the titration, as indicator. Repeat the operation without the substance being examined. The difference between the titrations represents the amount of sodium thiosulfate required. Each ml of 0.01M *sodium thiosulfate VS* is equivalent to 1.211 mg of $C_{14}H_{10}O_4$.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of anhydrous benzoyl peroxide.