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

Benzatropine Tablets

General Notices

Action and use

Anticholinergic.

DEFINITION

Benzatropine Tablets contain Benzatropine Mesilate.

The tablets comply with the requirements stated under Tablets and with the following requirements.

PRODUCTION

Risk assessment should be used to evaluate the potential for genotoxic methanesulfonate esters to be formed in the presence of low molecular weight alcohols. If a risk of methanesulfonate ester formation is identified through risk assessment, these impurities should not exceed the threshold of toxicological concern.

Content of benzatropine mesilate, $C_{21}H_{25}NO,CH_4O_3S$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. Shake a suitable quantity of the powdered tablets with 2M *hydrochloric acid* and filter. Dilute the filtrate with sufficient 2 M *hydrochloric acid* to produce a solution containing 0.1% w/v of Benzatropine Mesilate. The *light absorption* of the resulting solution, Appendix II B, in the range 230 to 350 nm exhibits two maxima, at 253 nm and 258 nm.
B. Extract a quantity of the powdered tablets containing 10 mg of Benzatropine Mesilate with 10 mL of *ethanol (96%)* and filter. Evaporate the filtrate to about 2 mL, pour into 5 mL of hot *picric acid solution R1* and allow to cool. The *melting point* of the precipitate, after drying at 105°, is about 185°, Appendix V A.

TESTS

Tropine

Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.

(1) Shake a quantity of the powdered tablets containing 20 mg of Benzatropine Mesilate with 4 mL of *acetone* for 5 minutes, centrifuge, evaporate 2 mL of the supernatant liquid to dryness and dissolve the residue in 0.5 mL of *acetone*.
(2) 0.010% w/v of *tropine* in *acetone*.

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 air, spray with *sodium iodobismuthate solution* and then with a 0.4% w/v solution of *sulfuric acid*.

MOBILE PHASE

15 volumes of 13.5M *ammonia* and 75 volumes of *ethanol (96%)*.

LIMITS

Any spot corresponding to tropine in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (2).

Uniformity of content

Tablets containing less than 2 mg and/or less than 2% w/w of Benzatropine Mesilate comply with the requirement stated under Tablets using the following method of analysis.

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

(1) Shake one tablet with 8 mL of the mobile phase for 5 minutes, add sufficient of the mobile phase to produce 10 mL, centrifuge for 5 minutes and use the supernatant liquid.
(2) 0.02% w/v of *benzatropine mesilate BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octylsilyl silica gel for chromatography* (10 µm) (Lichrosorb RP8 or Spherisorb C8 is suitable).
(b) Use isocratic elution (or gradient 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 259 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

35 volumes of *octylamine phosphate buffer pH 3.0* and 65 volumes of *acetonitrile*.

DETERMINATION OF CONTENT

Calculate the content of $C_{21}H_{25}NO,CH_4O_3S$ in each tablet using the declared content of $C_{21}H_{25}NO,CH_4O_3S$ in *benzatropine mesilate BPCRS*.

ASSAY

Weigh and powder 30 tablets. To a quantity of the powder containing 50 mg of Benzatropine Mesilate add 50 mL of *water* and shake for 15 minutes. Add 10 mL of a 50% w/v solution of *sodium hydroxide* and an excess of *sodium chloride* and extract with successive quantities of 50, 25, 25 and 25 mL of *ether*. Extract the combined ether layers with successive quantities of 25, 25, 25 and 15 mL of 2M *hydrochloric acid*, dilute the combined extracts to 100 mL with 2M *hydrochloric acid*, mix and filter if necessary. Measure the *absorbance* of the resulting solution at the maximum at 258 nm, Appendix II B. Calculate the content of $C_{21}H_{25}NO,CH_4O_3S$ from the *absorbance* obtained by repeating the operation using 50 mg of *benzatropine mesilate BPCRS* in place of the powdered tablets and from the declared content of $C_{21}H_{25}NO,CH_4O_3S$ in *benzatropine mesilate BPCRS*.