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

Mebeverine Tablets

General Notices

Action and use

Smooth muscle relaxant; antispasmodic.

DEFINITION

Mebeverine Tablets contain Mebeverine Hydrochloride.

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

Content of mebeverine hydrochloride, $C_{25}H_{35}NO_5$,HCl

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of powdered tablets containing 0.2 g of Mebeverine Hydrochloride in 20 mL of *water*, add 5 mL of 5M *sodium hydroxide* and extract with two 25-mL quantities of *dichloromethane*. Dry the combined extracts over *anhydrous sodium sulfate* and evaporate the solvent. The *infrared absorption spectrum* of the oily residue, Appendix II A, is concordant with the *reference spectrum* of mebeverine *(RS 208)*.

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

For film-coated tablets

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 75 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample (a 0.45-µm nylon filter is suitable), suitably diluted with the dissolution medium, if necessary, to produce a solution expected to contain 0.0024% w/v of Mebeverine Hydrochloride at the maximum at 265 nm, Appendix II B, using the medium in the reference cell.
(2) Measure the *absorbance* of a 0.0024% w/v solution of *mebeverine hydrochloride BPCRS* in the dissolution medium, using the medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of mebeverine hydrochloride, $C_{25}H_{35}NO_5$,HCl, in the medium from the absorbances obtained and using the declared content of $C_{25}H_{35}NO_5$,HCl in *mebeverine hydrochloride BPCRS*.

LIMITS

The amount of mebeverine hydrochloride released is not less than 75% (Q) of the stated amount.

For sugar-coated tablets

TEST CONDITIONS

(a) Use Apparatus 1, rotating the basket at 100 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 60 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample (a 0.45-µm nylon filter is suitable), suitably diluted with the dissolution medium, if necessary, to produce a solution expected to contain 0.0024% w/v of Mebeverine Hydrochloride at the maximum at 265 nm, Appendix II B, using the medium in the reference cell.
(2) Measure the *absorbance* of a 0.0024% w/v solution of *mebeverine hydrochloride BPCRS* in the dissolution medium, using the medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of mebeverine hydrochloride, $C_{25}H_{35}NO_5$,HCl, in the medium from the absorbances obtained and using the declared content of $C_{25}H_{35}NO_5$,HCl in *mebeverine hydrochloride BPCRS*.

LIMITS

The amount of mebeverine hydrochloride released is not less than 70% (Q) of the stated amount.

Related substances

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

Solution A 3 volumes of *acetonitrile* and 7 volumes of mobile phase A.

(1) Shake a quantity of powdered tablets containing 50 mg of Mebeverine Hydrochloride with 50 mL of solution A, mix with the aid of ultrasound and shake intermittently. Dilute to 100 mL, mix and filter (a 0.45-µm nylon filter is suitable).
(2) Dilute 1 volume of solution (1) to 100 volumes. Dilute 1 volume of the resulting solution to 5 volumes.
(3) 0.05% w/v of *mebeverine impurity standard BPCRS*.
(4) 0.0001% w/v of *mebeverine impurity C BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *base-deactivated end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Inertsil ODS-3 is suitable).
(b) Use gradient 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 263 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 1 volume of *triethylamine* and 1000 volumes of 0.38% w/v *ammonium acetate*, adjusted to pH 3.0 with *orthophosphoric acid*.

Mobile phase B *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-5	70	30	isocratic
5-15	70→30	30→70	linear gradient
15-25	30	70	isocratic
25-27	30→70	70→30	linear gradient
27-35	70	30	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to mebeverine (retention time about 12 minutes) are: impurity C, about 0.3 and impurity D, about 0.6.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurities C and D is at least 15;

in the chromatogram obtained with solution (4), the *signal-to-noise ratio* of the peak due to impurity C is at least 20.

LIMITS

Identify any peaks corresponding to impurities C and D in the chromatogram obtained with solution (1), using the chromatogram obtained with solution (3), and multiply the area of the peak corresponding to impurity D by a correction factor of 0.4.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity C is not greater than the area of the principal peak in the chromatogram obtained with solution (4) (0.2%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%).

The total impurity content is not greater than 1.0%.

Disregard any peak with an area less than half the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Mix, with the aid of ultrasound and intermittent shaking, a quantity of powdered tablets containing 25 mg of Mebeverine Hydrochloride in 20 mL of *methanol*. Dilute to 100 mL with the mobile phase and filter (a 0.45-µm nylon filter is suitable). Dilute 1 volume to 5 volumes with the mobile phase.
(2) A 0.025% w/v solution, prepared by dissolving 25 mg of *mebeverine hydrochloride BPCRS* in 20 mL of *methanol* then diluting to 100 mL with the mobile phase. Further dilute 1 volume of the solution to 5 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *base -deactivated end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Inertsil ODS-3 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 a column temperature of 25°.
(e) Use a detection wavelength of 263 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

380 volumes of *acetonitrile* and 620 volumes of a 0.38% w/v solution of *ammonium acetate*, previously adjusted to pH 5.2 using *glacial acetic acid*.

When the chromatograms are recorded under the prescribed conditions, the retention time of mebeverine is about 10 minutes.

DETERMINATION OF CONTENT

Calculate the content of mebeverine hydrochloride, $C_{25}H_{35}NO_5$,HCl, in the tablets from the chromatograms obtained and using the declared content of $C_{25}H_{35}NO_5$,HCl in *mebeverine hydrochloride BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities C and D listed under Mebeverine Hydrochloride.