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Mebeverine Prolonged-release Capsules

General Notices

Mebeverine Prolonged-release Capsules from different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable unless otherwise justified and authorised.

Action and use

Smooth muscle relaxant; antispasmodic.

DEFINITION

Mebeverine Prolonged-release Capsules contain Mebeverine Hydrochloride. They are formulated so that the Mebeverine Hydrochloride is released over a period of several hours.

The capsules comply with the requirements stated under Capsules and with the following requirements.

PRODUCTION

A suitable dissolution test is carried out to demonstrate the appropriate release of Mebeverine Hydrochloride. The dissolution profile reflects the *in vivo* performance which in turn is compatible with the dosage schedule recommended by the manufacturer.

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 capsule contents 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

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 capsule contents 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 the contents of 20 capsules. Mix, and powder if necessary. 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 capsule contents containing 25 mg of Mebeverine Hydrochloride in 70 mL of *methanol*. Dilute to 100 mL with *methanol* and filter (a 0.45-µm nylon filter is suitable). Dilute 1 volume to 5 volumes with the mobile phase.
(2) 0.025% w/v of *mebeverine hydrochloride BPCRS* in *methanol*. 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 0.38% w/v *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 capsules 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.