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Omeprazole Gastro-resistant Tablets

General Notices

Gastro-resistant Omeprazole Tablets

Action and use

Proton pump inhibitor; treatment of peptic ulcer disease.

DEFINITION

Omeprazole Gastro-resistant Tablets contain Omeprazole or Omeprazole Magnesium. They are covered with a gastro-resistant coating or prepared from granules or particles covered with a gastro-resistant coating.

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

Content of omeprazole, $C_{17}H_{19}N_3O_3S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

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

Solution A 11 volumes of 0.25M *trisodium orthophosphate*, 22 volumes of 0.5M *disodium hydrogen orthophosphate* and 67 volumes of *water*. Adjust to pH 11.0 with *orthophosphoric acid* or 10M *sodium hydroxide*.

Solution B 0.1 volumes of 10M *sodium hydroxide* and 10 volumes of *0.05M phosphate buffer solution pH 4.5*.

Solution C 5.2 volumes of 1M *anhydrous sodium dihydrogen orthophosphate* and 63.2 volumes of 0.5M *anhydrous disodium hydrogen orthophosphate* and dilute to 1000 volumes with *water*. Adjust to pH 7.6 with *orthophosphoric acid* or 10M *sodium hydroxide*.

First stage (pH 4.5)

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 100 revolutions per minute.
(b) Use 700 mL of *0.05M phosphate buffer solution pH 4.5*, at a temperature of 37°, as the medium.

PROCEDURE

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

(1) After 60 minutes withdraw 5 mL of the medium and filter (a 0.45-µm nylon filter is suitable). Dilute 1 volume of the filtrate to 5 volumes with solution A and retain the samples for analysis. Proceed immediately to the final stage.
(2) 0.0002% w/v of *omeprazole BPCRS* in a mixture of 1 volume of solution A and 9 volumes of *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 2 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Nucleosil C18 is suitable). Use a suitable guard column.
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.25 mL per minute.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 302 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

25 volumes of solution C, 35 volumes of *water* and 40 volumes of *acetonitrile*, adjusted to pH 7.6 with *orthophosphoric acid* or 10M *sodium hydroxide*.

When the chromatograms are recorded under the prescribed conditions, the retention time of omeprazole is about 4 minutes.

SYSTEM SUITABILITY

The *symmetry factor* of the peak due to omeprazole is not more than 2.0.

DETERMINATION OF CONTENT

Calculate the total content of $C_{17}H_{19}N_3O_3S$ in the medium using the declared content of $C_{17}H_{19}N_3O_3S$ in *omeprazole BPCRS*.

LIMITS

The amount of omeprazole released is not more than 10% of the stated amount.

Final stage (pH 6.8)

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 100 revolutions per minute.
(b) Within 1 minute of withdrawing the medium at completion of the first stage, add 200 mL of solution B, at a temperature of 37°, to the vessel.

PROCEDURE

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

(1) After 30 minutes withdraw a sample of the medium and filter (a 0.45-µm nylon filter is suitable). To a volume of the filtrate expected to contain the equivalent of 0.1 mg of omeprazole, add 1 volume of 0.25M *sodium hydroxide* and dilute to 25 volumes with solution A.
(2) 0.002% w/v of *omeprazole BPCRS* in a mixture of 1 volume of solution A and 9 volumes of *water*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under the first stage may be used.

SYSTEM SUITABILITY

The *symmetry factor* of the peak due to omeprazole is not more than 2.0.

DETERMINATION OF CONTENT

Calculate the total content of $C_{17}H_{19}N_3O_3S$ in the medium using the declared content of $C_{17}H_{19}N_3O_3S$ in *omeprazole BPCRS*.

LIMITS

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

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in mobile phase. The solutions should be prepared immediately before use.
(1) Disperse a quantity of the powdered tablets containing the equivalent of 24 mg of Omeprazole in 150 mL of mobile phase, mix with the aid of ultrasound for 30 minutes, dilute with sufficient mobile phase to produce 200 mL, mix and filter.
(2) Dilute 1 volume of solution (1) to 20 volumes. Dilute 1 volume of this solution to 10 volumes.
(3) 0.01% w/v each of *omeprazole BPCRS* and *omeprazole impurity D EPCRS*.
(4) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4.6 mm) packed with *octylsilyl silica gel for chromatography* (5 µm) (Nucleosil RP8 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 280 nm.
(f) Inject 40 µL of each solution.
(g) Allow the chromatography to proceed for 5 times the retention time of the peak due to omeprazole.

MOBILE PHASE

27 volumes of *acetonitrile* and 73 volumes of a 0.14% w/v solution of *disodium hydrogen orthophosphate*, previously adjusted to pH 7.6 with *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions the relative retentions with respect to omeprazole (retention time about 9 minutes) are: impurity D, about 0.8; impurity C, about 3.4.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity D and omeprazole is greater than 3.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak due to impurity D is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any other *secondary peak* is not greater than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any *secondary peaks* is not greater than four times the area of the principal peak in the chromatogram obtained with solution (2) (2.0%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

ASSAY

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

(1) Disperse a quantity of the powdered tablets containing 24 mg of Omeprazole in 150 mL of mobile phase, mix with the aid of ultrasound for 30 minutes, dilute with sufficient mobile phase to produce 200 mL, mix, filter and further dilute 1 volume to 10 volumes.
(2) 0.0012% w/v of *omeprazole BPCRS*.
(3) 0.01% w/v each of *omeprazole BPCRS* and *omeprazole impurity D EPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used but with a detection wavelength of 305 nm.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity D and omeprazole is greater than 3.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{17}H_{19}N_3O_3S$ in the tablets from the chromatograms obtained and using the declared content of $C_{17}H_{19}N_3O_3S$ in *omeprazole BPCRS*.

IMPURITIES

The impurities limited by this monograph include those listed under Omeprazole.