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Ranitidine Oral Solution

General Notices

Action and use

Histamine H_2 receptor antagonist; treatment of peptic ulcer disease.

DEFINITION

Ranitidine Oral Solution is a solution of Ranitidine Hydrochloride in a suitable vehicle.

The oral solution complies with the requirements stated under Oral Liquids and with the following requirements.

Content of ranitidine, $C_{13}H_{22}N_4O_3S$

90.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Prepare a solid phase extraction cartridge containing a C_{18} sorbent (Sep-Pak C_{18} cartridges are suitable) by passing 10 mL of *methanol* followed by 20 mL of 0.5M *ammonia* through the cartridge; attach the tip of a suitable syringe to the cartridge. Transfer a quantity of the oral solution containing the equivalent of 10 mg of ranitidine to the barrel of the syringe, add 2 mL of 0.5M *ammonia* to the syringe, insert the plunger and slowly force the mixture through the cartridge, discarding the eluant; repeat with two 4-mL quantities of 0.5M *ammonia* discarding the eluant. Pass two 5-mL quantities of a mixture of 25 volumes of 0.1M *hydrochloric acid* and 75 volumes of *methanol* through the cartridge and collect the eluant; add 40 mL of *absolute ethanol* to the collected eluant, evaporate the resulting solution to dryness at a temperature not exceeding 30° under reduced pressure and dissolve the residue in 1 mL of *methanol*.
(2) Prepare in the same manner as solution (1) using a solution containing 1.12% w/v of *ranitidine hydrochloride BPCRS* in *water* in place of the preparation being examined.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel* (Merck silica gel 60 plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 2 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air and expose to iodine vapour in a closed chamber until the spots are visible.

MOBILE PHASE

4 volumes of *water*, 8 volumes of 18M *ammonia*, 30 volumes of *propan-2-ol* and 50 volumes of *ethyl acetate*.

CONFIRMATION

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

B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is the same as that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Acidity or alkalinity

pH, 6.7 to 7.5, Appendix V L.

Related substances

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

(1) Prepare a solid phase extraction cartridge containing a C_{18} sorbent (Sep-Pak C_{18} cartridges are suitable) by passing 10 mL of *methanol* followed by 20 mL of 0.5M *ammonia* through the cartridge; attach the tip of a suitable syringe to the cartridge. Transfer a weighed quantity of the oral solution containing the equivalent of 15 mg of ranitidine to the barrel of the syringe, add 2 mL of 0.5M *ammonia* to the syringe, insert the plunger and slowly force the mixture through the cartridge, discarding the eluant; repeat with two 4 mL quantities of 0.5M *ammonia* discarding the eluant. Pass two 5-mL quantities of a mixture of 25 volumes of 0.1M *hydrochloric acid* and 75 volumes of *methanol* through the cartridge and collect the eluant; add 40 mL of *absolute ethanol* to the collected eluant, evaporate the resulting solution to dryness at a temperature not exceeding 30° under reduced pressure and dissolve the residue in 2 mL of *water*.
(2) Dilute 1 volume of solution (1) to 50 volumes with *water*.
(3) Dilute 1 volume of solution (1) to 100 volumes with *water*.
(4) Dilute 1 volume of solution (1) to 200 volumes with *water*.
(5) Dilute 1 volume of solution (3) to 5 volumes with *water*.
(6) Dissolve the contents of a vial of *ranitidine impurity J EPCRS* in 1 mL of a solution containing 0.15% w/v of *ranitidine hydrochloride BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *octadecylsilyl amorphous organosilica polymer* (3.5 µm) (XTerra MS C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 35°.
(e) Use a detection wavelength of 230 nm.
(f) Use an injection volume of 20 µL for each solution.

MOBILE PHASE

Buffer solution Adjust the pH of 950 mL of 0.05M *potassium dihydrogen orthophosphate* to 7.1 by adding *strong sodium hydroxide solution* and dilute to 1 litre.

Mobile phase A 2 volumes of *acetonitrile* and 98 volumes of buffer solution.

Mobile phase B 22 volumes of *acetonitrile* and 78 volumes of buffer solution.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-10	100→0	0→100	linear gradient
10-15	0	100	isocratic
15-16	0→100	100→0	linear gradient
16-20	100	0	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (6), the *resolution* between the two principal peaks is at least 1.5.

LIMITS

In the chromatogram obtained with solution (1):

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

the area of not more than one *secondary peak* is greater than the area of the principal peak in the chromatogram obtained with solution (3) (1%);

the area of not more than two other *secondary peaks* is greater than the area of the principal peak in the chromatogram obtained with solution (4) (0.5%);

the area of not more than two further *secondary peaks* is greater than the principal peak in solution (5) (0.2%);

the sum of the areas of all *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (5%).

Disregard any peak with an area less than 0.25 times the area of the principal peak in the chromatogram obtained with solution (5) (0.05%).

ASSAY

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

(1) Dilute a weighed quantity of the oral solution containing the equivalent of 10 mg of ranitidine with sufficient of the mobile phase to produce 100 mL.
(2) 0.0112% w/v of *ranitidine hydrochloride BPCRS* in the mobile phase.
(3) 0.0112% w/v of *ranitidine hydrochloride BPCRS* and 0.0002% w/v of *dimethyl{5-[2-(1-methylamino-2-nitrovinylamino)ethylsulfinylmethyl]furfuryl}amine BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) A stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (Partisil ODS 1 is suitable).
(b) Isocratic elution using the mobile phase described below.
(c) Flow rate of 2 mL per minute.
(d) Ambient column temperature.
(e) Detection wavelength of 322 nm.
(f) Injection volume of 20 µL for each solution.

MOBILE PHASE

15 volumes of 0.1M *ammonium acetate* and 85 volumes of *methanol*.

SYSTEM SUITABILITY

The assay is not valid unless the peak due to ranitidine in the chromatogram obtained with solution (3) shows baseline separation from the peak due to dimethyl{5-[2-(1-methylamino-2-nitrovinylamino)ethylsulfinylmethyl]furfuryl}amine.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral solution, Appendix V G, and calculate the content of $C_{13}H_{22}N_4O_3S$, weight in volume, using the declared content of $C_{13}H_{22}N_4O_3S$ in *ranitidine hydrochloride BPCRS*.

STORAGE

Ranitidine Oral Solution should be protected from light.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of ranitidine.