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

Hydroxycarbamide Capsules

General Notices

Action and use

Cytotoxic alkylating drug.

DEFINITION

Hydroxycarbamide Capsules contain Hydroxycarbamide.

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

Content of hydroxycarbamide, $CH_4N_2O_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Shake a quantity of the contents of the capsules containing 30 mg of Hydroxycarbamide with 10 mL of *methanol* and filter. Evaporate the filtrate to dryness and dry the residue at 60° at a pressure of 2 kPa for 3 hours. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of hydroxycarbamide *(RS 184)*.
B. In the Assay, the chromatogram obtained with solution (1) shows a peak with the same retention time as that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Urea

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

(1) Shake a quantity of the contents of the capsules containing 0.5 g of Hydroxycarbamide with 10 mL of *water* for 15 minutes and filter through a glass-fibre filter (Whatman GF/C is suitable).
(2) 0.025% w/v of *urea*.
(3) 5.0% w/v of *hydroxycarbamide BPCRS* and 0.025% w/v of *urea*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel*.
(b) Use the mobile phase as described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air, spray with a 1% w/v solution of *4-dimethylaminobenzaldehyde* in 1M *hydrochloric acid*.

MOBILE PHASE

1 volume of *pyridine*, 1 volume of *water* and 5 volumes of *ethyl acetate*. Shake, allow to separate and use the upper layer.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) shows two clearly separated spots.

LIMITS

Any spot corresponding to urea in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (2) (0.5%).

Hydroxylamine

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

(1) Shake a quantity of the contents of the capsules containing 0.1 g of Hydroxycarbamide with 8 mL of *water* for 5 minutes, add sufficient water to produce 10 mL and filter through a glass-fibre filter (Whatman GF/C is suitable).
(2) 1.0% w/v of *hydroxycarbamide BPCRS* and 0.02% w/v of *hydroxylamine hydrochloride*.
(3) 0.1% w/v of *hydroxycarbamide BPCRS* and 1.0% w/v of *hydroxylamine hydrochloride*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 214 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

5 volumes of *methanol* and 95 volumes of *water*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to hydroxycarbamide and hydroxylamine is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to hydroxylamine is not greater than the area of the corresponding peak in the chromatogram obtained with solution (2) (1%).

ASSAY

Weigh and powder the contents of 20 capsules. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in *water*.

(1) Shake a quantity of the capsule contents containing 1 g of Hydroxycarbamide with 450 mL of *water* for 5 minutes, mix for 30 minutes with the aid of ultrasound, add sufficient *water* to produce 500 mL and mix well. Filter through a glass-fibre filter (Whatman GF/C is suitable) and dilute 1 volume of the filtrate with 1 volume of *water*.
(2) 0.10% w/v of *hydroxycarbamide BPCRS*
(3) 0.10% w/v of *hydroxycarbamide BPCRS* and 0.4% w/v of *hydroxylamine hydrochloride*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS 2 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.5 mL per minute.
(d) Use an ambient column temperature.

(e) Use a detection wavelength of 214 nm.

(f) Inject 20 µL of each solution.

MOBILE PHASE

water.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between hydroxycarbamide and hydroxylamine hydrochloride is at least 1.0.

DETERMINATION OF CONTENT

Calculate the content of $CH_4N_2O_2$ in the capsules using the declared content of $CH_4N_2O_2$ in *hydroxycarbamide BPCRS*.

STORAGE

Hydroxycarbamide Capsules should be protected from moisture.