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

Calcium Folinate Tablets

General Notices

Action and use

Vitamin B component.

DEFINITION

Calcium Folinate Tablets contain Calcium Folinate Hydrate.

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

Content of folinic acid, $C_{20}H_{23}N_7O_7$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. To a quantity of the powdered tablets containing the equivalent of 180 mg of folinic acid add 10 mL of *water*, mix with the aid of ultrasound, and filter. Add 125 mg of *ammonium oxalate* to the filtrate, shake, and centrifuge until a clear supernatant liquid is obtained. To the supernatant add 1 mL of *methanol* and 3 drops of *hydrochloric acid*, and shake. If the preparation is cloudy, add *methanol* until a clear solution is obtained and filter, if necessary, to remove any undissolved material. Cool the preparation at 0° until a precipitate forms and centrifuge. The cooling and centrifuging steps may be repeated, if necessary, to increase the amount of precipitate collected. Decant the supernatant liquid and dissolve the precipitate in 2 mL of *methanol*. Evaporate to dryness under a current of air and dry the residue at 50° for 30 minutes. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of calcium folinate *(RS 368)*.
B. The powdered tablets yield reaction B characteristic of *calcium salts*, Appendix VI.

TESTS

Related substances

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

(1) Add 20 mL of *water* to a quantity of the powdered tablets containing the equivalent of 25 mg of folinic acid, shake for 15 minutes and dilute to 25 mL with *water*. Filter through a glass fibre filter (Whatman GF/C is suitable).
(2) Dilute 1 volume of solution (1) to 100 volumes with *water*.
(2) Dilute 1 volume of solution (1) to 100 volumes with *water*.
(3) 0.1% w/v of *calcium folinate BPCRS* in *water*.
(4) Dilute 1 volume of solution (2) to 10 volumes with *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil ODS is suitable).

(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 280 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1) allow the chromatography to proceed for 2.5 times the retention time of folinate.

MOBILE PHASE

220 mL of *methanol* and 780 mL of a solution containing 2.0 mL of *tetrabutylammonium hydroxide solution* and 2.2 g of *disodium hydrogen orthophosphate*, previously adjusted to pH 7.5 with 10% v/v *orthophosphoric acid*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the peaks corresponding to folinate and formylfolic acid is at least 2.2. If necessary, adjust the methanol content in the mobile phase.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to formylfolic acid is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the sum of the areas of any *secondary peaks*, excluding the peak corresponding to formylfolic acid, is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (2.5%).

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

ASSAY

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

(1) Add 200 mL of *water* to a quantity of the powdered tablets containing the equivalent of 25 mg of folinic acid, shake for 15 minutes and dilute to 250 mL with *water*. Filter through a glass fibre filter (Whatman GF/C is suitable).
(2) 0.011% w/v of *calcium folinate BPCRS* in *water*.
(3) 0.1% w/v of *calcium folinate BPCRS* in *water*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the peaks corresponding to folinate and formylfolic acid is at least 2.2. If necessary, adjust the methanol content in the mobile phase.

DETERMINATION OF CONTENT

Calculate the content of $C_{20}H_{23}N_7O_7$ in the tablets using the declared content of $C_{20}H_{21}CaN_7O_7$ in *calcium folinate BPCRS*. Each mg of $C_{20}H_{21}CaN_7O_7$ is equivalent to 0.9255 mg of $C_{20}H_{23}N_7O_7$.

STORAGE

Calcium Folinate Tablets should be stored at a temperature not exceeding 30°.

LABELLING

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