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Hydrocortisone Tablets

Details for the public consultation of this monograph are as follows:

EAG	Medicinal Chemicals 3
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Notes	New Monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. Assay The addition of either a resolution or peak-to-valley system suitability test is being considered

Action and use

Corticosteroid.

DEFINITION

Hydrocortisone tablets contain hydrocortisone.

The Tablets comply with the requirements stated under [Tablets](#) and with the following requirements.

Content of hydrocortisone, C₂₁H₃₀O₅

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 B: 0.138% w/v solution of sodium dihydrogen phosphate monohydrate adjusted to pH 3.0 using 85% w/w orthophosphoric acid.

TEST CONDITIONS

- (a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
- (b) Use 900 mL of 0.1M [hydrochloric acid](#), at a temperature of 37°, as the medium.

PROCEDURE

- (1) After 30 minutes withdraw a sample of the medium and filter (a 0.45µm nylon syringe filter is suitable). Use the filtered medium, diluted, if necessary, to produce a solution expected to contain 0.00028% w/v of hydrocortisone.
- (2) Dilute 1 volume of solution (2) from the Assay to 100 volumes with the medium to give a 0.00024% w/v solution of hydrocortisone BPCRS.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column 15 cm × 4.6 mm packed with base-deactivated octadecylsilylsilica gel for chromatography (5 µm) (Apollo C18 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 autosampler at temperature 8°.
- (e) Use an ambient column temperature.
- (f) Use a detection wavelength of 242 nm.
- (g) Inject 20 µL of each solution.

MOBILE PHASE

26 volumes of [acetonitrile](#) and 74 volumes of solution B.

When the chromatograms are recorded under the prescribed conditions, the retention time of hydrocortisone is about 12 minutes.

DETERMINATION OF CONTENT

Calculate the total content of hydrocortisone, $C_{21}H_{30}O_5$, in the medium from the chromatograms obtained and using the declared content of $C_{21}H_{30}O_5$, in [hydrocortisone BPCRS](#).

LIMITS

The amount of hydrocortisone released is not less than 75% (Q) of the stated amount in 30 minutes.

Related substances

Carry out the method for [liquid chromatography, Appendix III D](#), using the following solutions prepared in solution A.

Solution A: 40 volumes of [acetonitrile](#) and 60 volumes of [water](#).

- (1) Disperse a quantity of powdered tablets containing 20 mg of hydrocortisone with 7 ml. Dilute to 10 ml and mix with the aid of ultrasound, and filter (0.45 µm nylon filter is suitable).
- (2) Dilute 1 volume of solution (1) to 200 volumes.
- (3) 0.002% w/v [cortisone R](#) (impurity B), 0.004% w/v of [prednisolone BPCRS](#) (impurity A), 0.006% w/v of [Reichstein's substance S](#) (impurity F) and 0.008% w/v of [hydrocortisone acetate BPCRS](#) (impurity C). Dilute 1 volume to 10 volumes with solution (1).
- (4) 0.2% w/v of [hydrocortisone for peak identification CRS](#) (impurities D, E, G, H, I and N) and mix with the aid of ultrasound.
- (5) Dilute 1 volume of solution (2) to 5 volumes.

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) (YMC-Pack Pro C18 is suitable).
- (b) Use gradient elution and the mobile phases described below.
- (c) Use a flow rate of 0.8 mL per minute.
- (d) Use an ambient column temperature.
- (e) Use a detection wavelength of 254nm.
- (f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A [water](#).

Mobile phase B [acetonitrile](#).

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-18	74	26	isocratic
18-32	74→55	26→45	linear gradient
32-48	55→30	45→70	linear gradient
48-49	30→74	70→26	linear gradient
49-55	74	26	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the [peak-to-valley ratio](#) is at least 3.0, where *H_p* is the height above the baseline of the peak due to impurity A and *H_v* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to hydrocortisone.

The test is not valid unless, in the chromatogram obtained with solution (5), the signal-to-noise ratio of the peak due to impurity E is at least 30.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of hydrocortisone in solution (2).

For the reporting threshold, use the concentration of hydrocortisone in solution (5).

For peak identification, use solutions (3) and (4).

hydrocortisone retention time: about 24 minutes.

Relative retention: impurity D, about 0.2; impurity H, about 0.3; impurity I, about 0.5; impurity 1, about 0.79; impurity G, about 0.82; impurity E, about 0.86; impurity A, about 0.96; impurity B, about 1.1; impurity F, about 1.4; impurity C, about 1.5; impurity N, about 1.7. impurity; Impurity 3, about 1.8.

Correction factors: impurity D, multiply by 1.8; impurity E, multiply by 2.7; impurity 1, multiply by 1.3; impurity 3, multiply by 1.3.

LIMITS

- impurity C not more than 0.5%;
- impurity D not more than 0.5%;
- impurity E not more than 0.5%;
- impurity 3 not more than 0.5%;
- impurity G not more than 0.4%;
- impurity F not more than 0.3%;
- impurity 1 not more than 0.3%;
- unspecified impurities: for each impurity, not more than 0.2%;
- total impurities: not more than 2.0%;
- reporting threshold: 0.1%.

ASSAY

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

Solution B: 0.138% w/v solution of sodium dihydrogen phosphate monohydrate adjusted to pH 3.0 using 85% w/w orthophosphoric acid.

Solution C: 22 volumes of acetonitrile and 78 volumes of solution B.

- (1) To a quantity of powdered tablets containing 24 mg of Hydrocortisone add 2 mL of Solution B and swirl. Add 80 mL of solution C, mix with the aid of ultrasound and occasional shaking. Allow to cool, dilute to 100 mL with solution C and filter.
- (2) 0.024% w/v of [hydrocortisone BPCRS](#) in solution C.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used with the following modifications.

- (d) Use an ambient autosampler temperature.

DETERMINATION OF CONTENT

Calculate the content of hydrocortisone, $C_{21}H_{30}O_5$, in the tablets from the chromatograms obtained and using the declared content of $C_{21}H_{30}O_5$ in [hydrocortisone BPCRS](#).

Supporting information for Dissolution and Assay

In developing the Dissolution and Assay methods, geometric scaling of column dimensions and chromatographic parameters to the validated method conditions have been explored in order to reduce the solvent needed and the environmental impact. The "More resources" tab, available in the BP online monograph, provides additional information on the investigations carried out. Visit <https://www.pharmacopoeia.com/guidance/environmentalhub> for more information.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, B, C, D, E, F, G, H, I and N listed under [Hydrocortisone](#) and the following impurities 1 and 3.

 1. [systematic impurity name (short name)]

1. [systematic impurity name (short name)]

 3. [systematic impurity name (short name)]

3. [systematic impurity name (short name)]