EAG/Panel/Working Party	Antibiotics
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Notes: Revised Monograph. Changes made to the related substances, assay and identification methods.	

Griseofulvin Tablets

Griseofulvin Preparations

Action and use
Antifungal.

DEFINITION

Griseofulvin Tablets contain Griseofulvin.

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

Content of griseofulvin, $C_{17}H_{17}ClO_6$
95.0 to 105.0% of the stated amount.

IDENTIFICATION

Extract a quantity of the powdered tablets containing 0.125 g of Griseofulvin with 20 mL of *dichloromethane*, add 1 g of *anhydrous sodium sulfate*, shake and filter. Evaporate the filtrate to dryness and dry at a pressure not exceeding 0.7 kPa for 1 hour. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of griseofulvin *(RS 172)*.

TESTS

Dissolution
Comply with the requirements for Monographs of the British Pharmacopoeia in the dissolution test for tablets and capsules, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 100 revolutions per minute.

(b) Use 1000 mL of a 1.5% w/v solution of sodium dodecyl sulfate, at a temperature of 37°, as the medium.

PROCEDURE

After 45 minutes withdraw a 10 ml sample of the medium and filter. Measure the absorbance of the filtrate, suitably diluted if necessary with methanol (80%), at the maximum at 291 nm, Appendix II B, using a 1.5% w/v solution of sodium dodecyl sulfate in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of griseofulvin, $C_{17}H_{17}ClO_6$, in the medium taking 725 as the value of A(1%, 1 cm) at the maximum at 291 nm.

Related substances
Carry out the method for liquid chromatography, Appendix III D, using the following solutions in mobile phase B.

(1) Disperse a quantity of powdered tablets containing 250 mg of griseofulvin in mobile phase B and dilute to 500 mL.

(2) Dilute 1 volume of solution (1) to 100 volumes.

(3) 0.05% w/v of *griseofulvin for LC assay and identification EPCRS*.

(4) 0.05% w/v of *griseofulvin for system suitability EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Discovery C18 is suitable).

(b) Use gradient elution and the mobile phase described below.

(c) Use a flow rate of 1.0 mL per minute.

(d) Use a column temperature of 30°.

(e) Use a detection wavelength of 290 nm.

(f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile Phase A

20 volumes of 0.1 % v/v *anhydrous formic acid* adjusted to pH 4.5 with dilute *ammonia R2* and 80 volumes of *water*.

Mobile Phase B

15 volumes of *water*, 20 volumes of 0.1 % v/v *anhydrous formic acid* adjusted to pH 4.5 with *dilute ammonia R2* and 65 volumes of *acetonitrile R*.

Time D_t (dwell volume used for development of the method) + 1.6 mL (min)	Mobile phase A (per cent V/V)	Mobile phase B (per cent V/V)
0 - 3	50	50
3 - 13	50 → 40	50 → 60
13 - 16	40 → 10	60 → 90
16 - 24	10	90

When the chromatograms are recorded under the prescribed conditions the retention time relative to griseofulvin (retention time about 16 minutes) are: Impurity A, about 0.4, Impurity B, about 0.7, and impurity C, about 1.1.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *peak-to-valley ratio* is at least 3.0 where Hp is the height above the baseline of the peak due to impurity C and Hv is the height above the baseline of the lowest point of the curve separating this peak from the peak due to griseofulvin.

LIMITS

In the chromatogram obtained with solution (1):

Identify any peaks corresponding to impurity A and multiply the area of this peak by a correction factor of 0.6.

The area of any peak corresponding to impurity B is not greater than 3 times the area of the principal peak obtained with solution (2) (3%).

The area of any peak corresponding to impurity A is not greater than twice the area of the principal peak obtained with solution (2) (2%).

The area of any peak corresponding to impurity C is not greater than 0.75 times the area of the principal peak obtained with solution (2) (0.75%).

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

the sum of the areas of any such peaks is not greater than 4 times the area of the principal peak in the chromatogram obtained with solution (2) (5%).

Disregard any peaks due to excipients and any peak with an area less than 0.1 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

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

(1) Disperse a quantity of powdered tablets containing 250 mg of griseofulvin in mobile phase B and dilute to 500 mL.

(2) 0.05% w/v of *griseofulvin for LC assay and identification EPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

DETERMINATION OF CONTENT

Calculate the content of $C_{17}H_{17}ClO_6$ in the tablets using the declared content of $C_{17}H_{17}ClO_6$ in *griseofulvin for LC assay and identification EPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include A, B and C listed under Griseofulvin.