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Chloramphenicol Ear Drops

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

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Notes:	**Revised monograph** If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. **Identification:** New infrared procedure approved by BP Laboratory, TLC test removed. **Related Substances:** Test harmonised with Ph. Eur. monograph, providing better control of impurities. **Assay:** Test harmonised with Ph. Eur. related substances procedure.

Action and use

Antibacterial.

DEFINITION

Chloramphenicol Ear Drops are a solution of Chloramphenicol in a suitable vehicle.

The ear drops comply with the requirements stated under Ear Preparations and with the following requirements.

Content of chloramphenicol, $C_{11}H_{12}Cl_2N_2O_5$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. Extract a quantity of the ear drops containing 0.1 g of Chloramphenicol with 60 mL of *water* and 40 mL of *ethyl acetate*. Evaporate to dryness under a stream of nitrogen. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the reference spectrum of chloramphenicol *(RS XXX)*.

B. Dilute a volume of the ear drops containing 50 mg of Chloramphenicol to 10 mL with *ethanol (50%)*. To 2 mL add 4.5 mL of 1M *sulfuric acid* and 50 mg of *zinc powder* and allow to stand for 10 minutes. Decant the supernatant liquid or filter if necessary. Cool the resulting solution in ice and add 0.5 mL of *sodium nitrite solution* and, after 2 minutes, 1 g of *urea* followed by 1 mL of *2-naphthol*

solution and 2 mL of 10M *sodium hydroxide*; a red colour is produced. Repeat the test omitting the zinc powder; no red colour is produced.

TESTS

Related substances

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

(1) Shake a quantity of the ear drops containing 25 mg of Chloramphenicol with 5 mL of *methanol*, add sufficient mobile phase A to produce 50 mL, mix and filter.

(2) 0.05 % w/v *chloramphenicol BPCRS* prepared by dissolving 25 mg in 5 mL of *methanol* then diluting to 50 mL in mobile phase A. Dilute 1 volume to 100 volumes with mobile phase A.

(3) Solution of 0.0025% w/v *4-nitrobenzaldehyde* and 0.05% w/v *chloramphenicol for peak identification EPCRS* in mobile phase A.

(4) Dilute 1 volume of solution (2) to 10 volumes with mobile phase A.

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) (Hypersil BDS C18 is suitable).

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

(c) Use a flow rate of 1 mL per minute.

(d) Use a column temperature of 25°.

(e) Use a sampler temperature of 8°.

(f) Use a detection wavelength of 277 nm.

(g) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 32 volumes of *methanol* and 68 volumes of a solution of 0.2% w/v *sodium heptansulfonate*, 0.68% w/v *potassium dihydrogen phosphate* and 0.5% v/v *triethylamine*, previously adjusted to pH 2.5 with *orthophosphoric acid*.

Mobile phase B *methanol*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-13	100	0	isocratic
13-25	100→60	0→40	linear gradient
25-33	60	40	isocratic
33-34	60→100	40→0	linear gradient
34-40	100	0	re-equilibration

When the chromatograms are recorded under the prescribed conditions the relative retentions with reference to chloramphenicol (retention time about 14 minutes) are impurity A, about 0.7; impurity B, about 0.9.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks corresponding to impurity B and chloramphenicol is at least 2.0.

LIMITS

Identify any peaks in the chromatogram obtained with solution (1) corresponding to impurities A and B using the chromatogram obtained with solution (3) and the chromatogram supplied with chloramphenicol for impurity identification EPCRS. Multiply the area of any peak corresponding to impurity A by a correction factor of 0.7.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (2.0%);

the area of any other secondary peak is not greater than twice the area of the principal peak in the chromatogram obtained with solution (4) (0.2%);

the sum of the areas of any secondary peaks 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 the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

ASSAY

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

(1) Disperse a quantity of the ear drops containing 100 mg of Chloramphenicol in 10 mL of *methanol*. Dilute to 100 mL in mobile phase A, mix and filter. Dilute 1 volume of the resulting solution to 10 volumes in mobile phase A.
(2) 0.01% w/v of *chloramphenicol BPCRS* in mobile phase A.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related Substances may be used.

DETERMINATION OF CONTENT

Calculate the content of chloramphenicol, $C_{11}H_{12}Cl_2N_2O_5$, in the ear drops using the declared content of $C_{11}H_{12}Cl_2N_2O_5$ in chloramphenicol BPCRS.

STORAGE

Chloramphenicol Ear Drops should be protected from light.