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

Hydrocortisone and Clioquinol Ointment

General Notices

Action and use

Corticosteroid.

DEFINITION

Hydrocortisone and Clioquinol Ointment contains Hydrocortisone and Clioquinol, the latter in *very fine powder*, in a suitable basis.

The ointment complies with the requirements stated under Topical Semi-solid Preparations and with the following requirements.

Content of hydrocortisone, $C_{21}H_{30}O_5$

92.5 to 107.5% of the stated amount.

Content of clioquinol, C_9H_5ClINO

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using *silica gel G* as the coating substance and a mixture of 77 volumes of *dichloromethane*, 15 volumes of *ether*, 8 volumes of *methanol* and 1.2 volumes of *water* as the mobile phase. Apply separately to the plate 5 µl of each of the following solutions. For solution (1) disperse, by warming and shaking, a quantity of the ointment containing 2.5 g of Hydrocortisone in 10 ml of *ethanol (96%)*, cool, allow to stand at 0° for 30 minutes, filter and use the filtrate. Solution (2) contains 0.25% w/v of *hydrocortisone BPCRS* in *ethanol (96%)*. For solution (3) dissolve 12.5 mg of *hydrocortisone BPCRS* in 5 ml of solution (1). After removal of the plate, allow it to dry in air and spray with *alkaline tetrazolium blue solution*. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2). The principal spot in the chromatogram obtained with solution (3) appears as a single, compact spot.
B. In the Assay for hydrocortisone the chromatogram obtained with solution (3) shows a peak with the same retention time as the peak due to hydrocortisone in the chromatogram obtained with solution (1).
C. Fuse a quantity of the ointment containing 0.1 g of Clioquinol with *anhydrous sodium carbonate*, dissolve the fused mass in *water* and acidify with 2M *nitric acid*. Add *silver nitrate solution*; a pale yellow precipitate is produced which is insoluble in 5M *ammonia*. Add 5M *ammonia* until the solution becomes alkaline, boil gently, filter and acidify the filtrate with 2M *nitric acid*; a white precipitate is produced which darkens on exposure to light.

ASSAY

For hydrocortisone

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. For solution (1) dissolve 5 mg of *hydrocortisone BPCRS* in 5 ml of a 4% v/v solution of *bromobenzene* (internal standard) in *methanol* and dilute to 50 ml with *methanol (80%)*. For solution (2) add 30 ml of *2,2,4-trimethylpentane* to a quantity of the ointment containing 10 mg of Hydrocortisone and warm on a water bath until the preparation has melted. Extract the warm mixture with successive quantities of 30, 20 and 20 ml of *methanol (80%)*, combine the aqueous methanolic layers, cool to about 20° and dilute to 100 ml with the same solvent. Prepare solution (3) in the same manner as solution (2) but adding 10 ml of a 4% v/v solution of *bromobenzene* in *methanol* to the cooled methanolic extract.

The chromatographic procedure may be carried out using (a) a stainless steel column (25 cm × 5 mm) packed with *octadecylsilyl silica gel for chromatography* (Spherisorb ODS 1 is suitable), (b) *methanol (65%)* as the mobile phase with a flow rate of 1 ml per minute and (c) a detection wavelength of 242 nm.

Calculate the content of $C_{21}H_{30}O_5$ in the ointment using the declared content of $C_{21}H_{30}O_5$ in *hydrocortisone BPCRS*.

For clioquinol

To a quantity containing 25 mg of Clioquinol add 80 ml of a hot mixture of 24 volumes of *2-methoxy-ethanol* and 6 volumes of *water* and heat on a water bath for 5 minutes. Cool in ice for 10 minutes, allow to warm to room temperature, dilute to 100 ml with the aqueous methoxyethanol, mix and filter. To 10 ml of the filtrate add 10 ml of *2-methoxyethanol* and 2 ml of a solution prepared by dissolving 0.5 g of *iron(III) chloride hexahydrate* in 80 ml of *2-methoxyethanol* and adding 0.1 ml of *hydrochloric acid* and sufficient *2-methoxyethanol* to produce 100 ml. Dilute the solution to 25 ml with *2-methoxyethanol* and measure the *absorbance* of the resulting solution at the maximum at 650 nm, Appendix II B, using in the reference cell a solution prepared by treating 10 ml of the aqueous methoxyethanol in the same manner beginning at the words ‘add 10 ml of *2-methoxyethanol*…’.

Repeat the operation beginning at the words ‘add 10 ml of *2-methoxyethanol*…’ using 10 ml of a solution prepared in the following manner. Dissolve 0.125 g of *clioquinol BPCRS* in sufficient *2-methoxyethanol* to produce 50 ml, warming to effect solution; add 1 ml of *water* to 5 ml of the solution and add sufficient of a mixture of 6 volumes of *water* and 24 volumes of *2-methoxyethanol* to produce 50 ml. Calculate the content of C_9H_5ClINO from the *absorbances* obtained using the declared content of C_9H_5ClINO in *clioquinol BPCRS*.

STORAGE

Hydrocortisone and Clioquinol Ointment should be protected from light.