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Hydrocortisone Sodium Phosphate Injection

General Notices

Action and use

Corticosteroid.

DEFINITION

Hydrocortisone Sodium Phosphate Injection is a sterile solution of Hydrocortisone Sodium Phosphate in Water for Injections.

The injection complies with the requirements stated under Parenteral Preparations and with the following requirements.

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

92.5 to 107.5% of the stated amount.

CHARACTERISTICS

A colourless or very pale yellow solution.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Dilute a volume of the injection containing the equivalent of 0.25 g of hydrocortisone to 100 mL with *water*.
(2) 0.34% w/v of *hydrocortisone sodium phosphate BPCRS* in *methanol*.
(3) A mixture of equal volumes of solutions (1) and (2).
(4) A mixture of equal volumes of solution (1) and a 0.25% w/v solution of *betamethasone sodium phosphate BPCRS* in *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel G*.
(b) Use the mobile phase as described below.
(c) Apply 5 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow to dry in air until the solvent has evaporated, spray with *ethanolic sulfuric acid (20%)*, heat at 120° for 10 minutes and examine under *ultraviolet light (365 nm)*.

MOBILE PHASE

A freshly prepared mixture of 20 volumes of *acetic anhydride*, 20 volumes of *water* *and* 60 volumes of *butan-1-ol*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position and colour 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.

The chromatogram obtained with solution (4) exhibits two principal spots with almost identical Rf values.

B. Evaporate 0.1 mL to dryness on a water bath and dissolve the residue in 2 mL of *sulfuric acid*. A yellowish green fluorescence is produced immediately (distinction from betamethasone sodium phosphate, dexamethasone sodium phosphate and prednisolone sodium phosphate).

TESTS

Alkalinity

pH, 7.5 to 8.5, Appendix V L.

Related substances

Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.

(1) Dilute a volume of the injection with *water* to contain the equivalent of 0.75% w/v of hydrocortisone.
(2) 1.0% w/v of *hydrocortisone sodium phosphate BPCRS* in *methanol*.
(3) 0.020% w/v of *hydrocortisone BPCRS* in *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel* GF_{254}.
(b) Use the mobile phase as described below.
(c) Apply 2 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow to dry in air for 5 minutes and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

1.2 volumes of *water*, 8 volumes of *methanol*, 15 volumes of *ether* *and* 77 volumes of *dichloromethane*.

LIMITS

Any *secondary spot* in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (3).

ASSAY

Dilute a volume containing the equivalent of 0.2 g of hydrocortisone to 1000 mL with *water*. To 5 mL add 15 mL of *water*, 2.5 g of *sodium chloride* and 0.5 mL of *hydrochloric acid* and extract with three 25-mL quantities of *chloroform*. Wash each chloroform layer with the same 1 mL quantity of 0.1M *hydrochloric acid*, add the washings to the aqueous solution and discard the chloroform. Extract the aqueous solution with two 10-mL quantities of *tributyl orthophosphate*, discard the aqueous phase and extract the combined tributyl phosphate solutions with two 25-mL quantities of a solution containing 10% w/v of *sodium chloride* and 1% w/v of *anhydrous disodium hydrogen orthophosphate*. Filter the extracts successively through absorbent cotton and wash the filter with 10 mL of the chloride–phosphate solution. Dilute the combined filtrates to 100 mL with the chloride–phosphate solution and measure the *absorbance* of the resulting solution at the maximum at 248 nm, Appendix II B, using in the reference cell a solution prepared in the same manner but using 20 mL of a solution containing 2.5 g of *sodium chloride* and 0.5 mL of *hydrochloric acid* and beginning at the words ‘Extract the aqueous solution…’. Calculate the content of hydrocortisone sodium phosphate as $C_{21}H_{30}O_5$ taking 447 as the value of A(1%, 1 cm) at the maximum at 248 nm.

STORAGE

Hydrocortisone Sodium Phosphate Injection should be protected from light. The injection should not be allowed to freeze.

LABELLING

The strength is stated in terms of the equivalent amount of hydrocortisone in a suitable dose-volume.