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

Kaolin and Morphine Mixture

General Notices

Kaolin and Morphine Oral Suspension

DEFINITION

Kaolin and Morphine Mixture is an *oral suspension* containing 0.00675% w/v Morphine Hydrochloride, 20% w/v of Light Kaolin or Light Kaolin (Natural) and 5% w/v of Sodium Bicarbonate in a suitable vehicle.

It should be recently prepared unless the kaolin has been sterilised.

The mixture complies with the requirements stated under Oral Liquids and with the following requirements.

Content of sodium bicarbonate, $NaHCO_3$

4.65 to 5.35% w/v.

Content of anhydrous morphine, $C_{17}H_{19}NO_3$

0.0055 to 0.0080% w/v.

IDENTIFICATION

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

(1) Centrifuge 10 mL of the preparation, reserving the supernatant liquid. Extract the residue with four 10-mL quantities of a mixture of 38 mL of *acetone* and 2 mL of 5M *ammonia*, centrifuging between each extraction, and evaporate the combined extracts on a water bath to about 5 mL. Mix with the reserved supernatant liquid, add 10 mL of 1M *sulfuric acid*, shake with two 10-mL quantities of *chloroform* and discard the chloroform. Add sufficient 5M *ammonia* to make the aqueous solution alkaline to *litmus paper*, extract with three 10-mL quantities of a mixture of equal volumes of *chloroform* and *ethanol (96%)*, evaporate to dryness and dissolve the residue in 0.5 mL of *ethanol (96%)*.
(2) 0.10% w/v of *morphine hydrochloride*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel*.
(b) Use the mobile phase as described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, heat at 105° to 110° for 30 minutes, allow to cool and spray with *dilute potassium iodobismuthate solution*.

MOBILE PHASE

10 volumes of *diethylamine*, 20 volumes of *ethyl acetate* and 70 volumes of *toluene*.

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).

TESTS

Acid-insoluble matter

13.8 to 18.4% w/w when determined by the following method. To 3 g add 15 mL of *water*, cautiously add sufficient *2M hydrochloric acid* to make the suspension acidic to *litmus paper*, boil for 5 minutes, replacing the water lost by evaporation, cool and filter the supernatant liquid. Boil the residue with 20 mL of *water* and 10 mL of *2M hydrochloric acid*, cool, filter through the same filter and wash the residue with *water* until the washings are free from chloride. Dry and ignite the residue to constant weight at red heat.

ASSAY

For sodium bicarbonate

Boil 20 mL with 40 mL of *water* for 5 minutes, replacing the water lost by evaporation, add 50 mL of *ethanol (96%)* previously neutralised to *methyl red solution* and allow to stand for 1 hour. Filter and wash the residue with 100 mL of a mixture of equal volumes of the neutralised ethanol and *water*. Add 50 mL of *0.5M hydrochloric acid VS* to the combined filtrate and washings, boil, cool and titrate the excess of hydrochloric acid with *0.5M sodium hydroxide VS* using *methyl red solution* as indicator. Each mL of *0.5M hydrochloric acid VS* is equivalent to 42.00 mg of $NaHCO_3$.

For anhydrous morphine

Centrifuge 25 mL, reserving the supernatant liquid, and extract the residue with three 25-mL quantities of *ethanol (96%)*, centrifuging between each extraction and reserving each supernatant liquid. Add 40 mL of *water* and 7 mL of 5M *ammonia* to the combined supernatant liquids and extract the mixture with three 30-mL quantities of *chloroform*. Gently shake each extract with the same 15 mL of a mixture of 2 volumes of *water* and 1 volume of *ethanol (96%)* and discard the aqueous ethanol. Evaporate the combined chloroform solutions just to dryness, warm the residue with 10 mL of 1M *hydrochloric acid*, cool the solution, which may be slightly cloudy, add sufficient *water* to produce 50 mL and filter (Whatman No. 42 paper is suitable). To 20 mL of the filtrate add 8 mL of a freshly prepared 1% w/v solution of *sodium nitrite*, allow to stand in the dark for 15 minutes, add 12 mL of 5M *ammonia* and sufficient *water* to produce 50 mL and measure the *absorbance* of a 4-cm layer at 442 nm without delay, Appendix II B. Use in the reference cell a solution prepared in the same manner but using *water* in place of the sodium nitrite solution. Calculate the content of anhydrous morphine taking 124 as the value of A(1%, 1 cm) at the maximum at 442 nm.

STORAGE

Kaolin and Morphine Mixture should be kept in well-filled glass containers.