Diethylcarbamazine dihydrogen citrate tablets (Diethylcarbamazini dihydrogenocitratis compressi)

Category. Antifilarial drug.

Storage. Diethylcarbamazine dihydrogen citrate tablets should be kept in a tightly closed container.

Additional information. Strengths in the current WHO Model list of essential medicines: 50 mg, 100 mg (dihydrogen citrate). Strengths in the current WHO Model list of essential medicines for children: 50 mg, 100 mg (dihydrogen citrate).

Requirements

Comply with the monograph for *Tablets*.

Diethylcarbamazine dihydrogen citrate tablets contain not less than 93.0% and not more than 107.0% of the amount of $C_{10}H_{21}N_3O,C_6H_8O_7$ stated on the label.

Identity tests

-Either tests A and C or tests B and C may be applied.

A. To a quantity of the powdered tablets equivalent to 0.15 g of Diethylcarbamazine dihydrogen citrate add 15 mL of ethanol (~750 g/l) TS, shake for 5 minutes, filter and evaporate the filtrate to dryness. To the residue add 10 mL of sodium hydroxide (~80 g/l) TS and extract with three 10 mL quantities of chloroform R. Dry the combined extracts over anhydrous sodium sulfate R, filter, evaporate the filtrates and carry out the examination as described under *1.7 Spectrophotometry in the infrared region*. The infrared absorption spectrum is concordant with the spectrum obtained from diethylcarbamazine dihydrogen citrate RS similarly treated or with the *reference spectrum* of diethylcarbamazine.

B. To a quantity of the powdered tablets equivalent to 0.2 g of Diethylcarbamazine dihydrogen citrate add 10 mL of water, shake and filter. Transfer the filtrate to a separatory funnel, add 1 mL of sodium hydroxide (~400 g/l) TS and extract with 20 mL, 15 mL and 10 mL of chloroform R. Keep the aqueous layer for test C. Evaporate the combined chloroform extracts on a water-bath and, towards the end, by drying with the aid of a current of air. Dissolve the oily residue in 10 mL of ethyl acetate R, warming the mixture to 50 °C, and pour it into 2 mL of a solution containing 1 g of maleic acid R in 10 mL of acetone R, warming again to 50 °C. Cool, rub the sides of the tube with a glass rod to induce crystallization, collect the white precipitate on a sintered-glass filter, wash twice with 1 mL of acetone R and once with 5 mL of ethyl acetate R and dry in a desiccator; melting point, 126-128 °C.

C. Filter the aqueous layer from test B. Add 1 drop of phenolphthalein/ethanol TS and neutralize with sulfuric acid (~100 g/l) TS. Then add 2 mL of mercuric sulfate TS, heat to boiling and add, drop by drop, potassium permanganate (10 g/l) TS; the violet colour is discharged and a white precipitate is produced.

***N*-Methylpiperazine.** Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography using silica gel R1 as the coating substance and a mixture of 6 volumes of ethanol (~750 g/l) TS, 3 volumes of glacial acetic acid R and 1 volume of water as the mobile phase. Apply separately to the plate 5 µl of each of the following two solutions. For solution (A) shake a quantity of the powdered tablets equivalent to 0.5 g of Diethylcarbamazine dihydrogen citrate with 10 mL of methanol R, filter and use the clear filtrate. For solution (B) dissolve 5 mg of *N*-methylpiperazine R in 100 mL of methanol R. After removing the plate from the chromatographic chamber allow it to dry in air, spray with a mixture of 3 volumes of platinic chloride (60 g/l) TS, 97 volumes of water and 100 volumes of potassium iodide (60 g/l) TS and examine the chromatogram in daylight.

The spot obtained with solution B is more intense than any spot, corresponding in position and appearance, obtained with solution A.

Assay

Weigh and powder 20 tablets. Transfer a quantity of the powder equivalent to about 0.75 g of Diethylcarbamazine dihydrogen citrate, accurately weighed, to a separatory funnel, add 10 mL of water and 10 mL of sodium hydroxide (~200 g/l) TS and shake to dissolve. Extract with four 25 mL quantities of chloroform R, washing each extract with the same two 20 mL quantities of water, and with a third quantity if the second is alkaline to phenolphthalein/ ethanol TS. Extract the combined chloroform extracts with 25 mL of sulfuric acid (0.05 mol/l) VS and then with 15 mL and 10 mL of water. Combine the acid and water extracts, warm to remove the chloroform, cool and back-titrate the excess of acid with sodium hydroxide (0.1 mol/l) VS using bromocresol green/ethanol TS as indicator.

Each mL of sulfuric acid (0.05 mol/l) VS is equivalent to 39.14 mg of $C_{10}H_{21}N_3O,C_6H_8O_7$.