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Mebendazole Oral Suspension

General Notices

Action and use

Benzimidazole antihelminthic.

DEFINITION

Mebendazole Oral Suspension is a suspension of Mebendazole in a suitable vehicle.

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

PRODUCTION

The formulation and production of Mebendazole Oral Suspension are designed to control and minimise the conversion of the polymorphic form of Mebendazole from C to A. They ensure that, at any stage of the life cycle of the product, when tested by a suitable method the Mebendazole in the oral suspension is predominantly in the form of polymorph C. The acceptable crystalline form corresponds to *mebendazole EPCRS*

Content of mebendazole, $C_{16}H_{13}N_3O_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the suspension containing 50 mg of Mebendazole with 20 mL of *water*. Filter, retain the residue and wash with three 10-mL quantities of *water* and dry overnight under vacuum at room temperature. The *infrared absorption spectrum* of the residue, Appendix II A, at 3405 cm^{-1} and 1720 cm^{-1} is concordant with the mebendazole polymorph C (*RS 503*). The presence of different polymorphic forms is indicated by differences in the spectra at 3405 cm^{-1} and 1720 cm^{-1}.

TESTS

Acidity

pH, 4.5 to 6.5, Appendix V L.

Related substances

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

(1) Shake a quantity of the oral suspension containing 50 mg of Mebendazole with 30 mL of *formic acid* and 30 mL of *methanol* (60%). Add sufficient *methanol* (60%) to produce 100 mL, filter (Acrodisc 0.45-µm GxF glass fiber PVDF is suitable), and use the filtrate.

(2) Dilute 1 volume of solution (1) to 100 volumes with *methanol* (60%). Dilute 1 volume of the resulting solution to 4 volumes with *methanol* (60%).
(3) To 5 mg of *mebendazole BPCRS* add 5 mL of *methanol* and 1 mL of 1M *sodium hydroxide*. Heat in a water bath at 60° for 1 hour, cool to room temperature, and adjust to pH 7 with 1M *hydrochloric acid*. Dilute to 100 mL with *methanol* and mix (generation of impurity A). To 1 volume of this solution, add 1 mL of 0.1% w/v of *methyl parahydroxybenzoate* in *methanol* and dilute to 100 volumes of *methanol (60%)*.
(4) 0.1% w/v of *mebendazole for system suitability EPCRS* in *dimethylformamide*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *base-deactivated octadecylsilyl silica gel for chromatography* (5 µm) (Zorbax SB-C18 is suitable)
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 40°.
(e) Use an autosampler temperature of 5°.
(f) Use a detection wavelength of 250 nm.
(g) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 0.025% v/v of *trifluoroacetic acid* in *water*.

Mobile phase B *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-20	90→70	10→30	linear gradient
20-29	70→30	30→70	linear gradient
29-30	30→90	70→10	linear gradient
30-35	90	10	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retention times with reference to mebendazole (retention time about 17 minutes) are: methyl parahydroxybenzoate, about 0.66; impurity A, about 0.69; impurity C, about 0.74; impurity B, about 0.9; impurity D, about 1.1; impurity E, about 1.20; impurity F, about 1.23; impurity G, about 1.5.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (3), the *resolution* between the peaks due to methyl parahydroxybenzoate and mebendazole impurity A is at least 2.0;

in the chromatogram obtained with solution (2), the *signal-to-noise ratio* of the peak due to mebendazole is at least 25.

LIMITS

Identify any peak in solution (1) corresponding to impurity G using the chromatogram obtained with solution (4) and multiply the area of this peak by a correction factor of 1.4.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity G is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.25%);

the sum of the areas of all *secondary peaks* is not greater than 4 times the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

Disregard any peak due to methyl parahydroxybenzoate and any peak with an area less than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

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

(1) Shake a weighed quantity of the oral suspension containing 50 mg of Mebendazole with 30 mL of *formic acid* and 30 mL of *methanol* (60%). Add sufficient *methanol* (60%) to produce 100 mL. Dilute 1 volume of the resulting solution to 5 volumes with *methanol* (60%). Filter (Acrodisc 0.45-µm GxF glass fiber PVDF is suitable) and use the filtrate.
(2) 0.01% w/v of *mebendazole BPCRS* in *dimethylformamide*.
(3) 0.01% w/v each of *mebendazole for system suitability EPCRS* and *methyl parahydroxybenzoate* in *dimethylformamide*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to methyl parahydroxybenzoate and mebendazole impurity A is at least 2.0.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral suspension, Appendix V G, and calculate the content of $C_{16}H_{13}N_3O_3$, weight in volume, using the declared content of $C_{16}H_{13}N_3O_3$ in *mebendazole BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Mebendazole.