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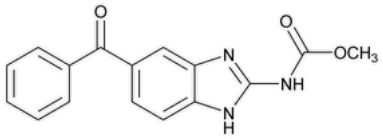
Mebendazole



$C_{16}H_{13}N_3O_3$ 295.29

Carbamic acid, (5-benzoyl-1*H*-benzimidazol-2-yl), methyl ester;

Methyl 5-benzoyl-2-benzimidazolecarbamate CAS RN®: 31431-39-7; UNII: 81G6I5V05I.

DEFINITION

Mebendazole contains NLT 98.0% and NMT 102.0% of mebendazole ($C_{16}H_{13}N_3O_3$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: 7.5 g/L of ammonium acetate

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
15	70	30
20	10	90
25	10	90
26	80	20
30	80	20

Diluent: Acetonitrile and water (50:50)

System suitability solution: 50 µg/mL of USP Mebendazole RS and 2.5 µg/mL of USP Mebendazole Related Compound D RS in *Diluent*. Sonicate in *Diluent* using 80% of the final volume at 45°–50° for 10 min. Dilute with *Diluent* to final volume.

Standard solution: 0.05 mg/mL of USP Mebendazole RS in *Diluent*. Sonicate in *Diluent* using 80% of the final volume at 45°–50° for 10 min. Dilute with *Diluent* to final volume.

Sample solution: 0.05 mg/mL of Mebendazole in *Diluent*. Sonicate in *Diluent* using 80% of the final volume at 45°–50° for 10 min. Dilute with *Diluent* to final volume.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 250 nm

Column: 4.6-mm × 10-cm; 3-µm packing L1

Column temperature: 40°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times of mebendazole and mebendazole related compound D are 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 5.0 between mebendazole and mebendazole related compound D, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of mebendazole ($C_{16}H_{13}N_3O_3$) in the portion of Mebendazole taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of mebendazole from the *Sample solution*

r_S = peak response of mebendazole from the *Standard solution*

C_S = concentration of USP Mebendazole RS in the *Standard solution* (mg/mL)

C_U = concentration of Mebendazole in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%
- **ORGANIC IMPURITIES**

Solution A, Solution B, Mobile phase, Diluent, System suitability solution, Sample solution, and **Chromatographic system:** Prepare as directed in the *Assay*.

Standard solution: 2.5 µg/mL of USP Mebendazole RS in *Diluent*

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 5.0 between the mebendazole and mebendazole related compound D peaks

Relative standard deviation: NMT 1.0% for the mebendazole peak and NMT 5.0% for the mebendazole related compound D peak

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of each impurity in the portion of Mebendazole taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of mebendazole from the *Standard solution*

C_S = concentration of USP Mebendazole RS in the *Standard solution* (mg/mL)

C_U = concentration of Mebendazole in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. Disregard peaks less than 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
2-Amino mebendazole[a]	0.46	1.0	0.25
2-Hydroxy mebendazole[b]	0.53	1.0	0.25

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
2-Amino-1-methyl mebendazole[c]	0.67	1.0	0.25
Mebendazole	1.0	—	—
Mebendazole related compound D	1.1	1.0	0.25
Ethyl mebendazole[d]	1.3	1.0	0.25
Toluoyl mebendazole[e]	1.4	1.0	0.25
Mebendazole dimer[f]	1.6	0.71	0.5
Any other unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

[a] 2-Amino-5-benzoylbenzimidazole.

[b] 5-Benzoyl-2-hydroxybenzimidazole.

[c] 2-Amino-5-benzoyl-1-methylbenzimidazole.

[d] Ethyl (5-benzoyl-1*H*-benzimidazol-2-yl)carbamate.

[e] Methyl 5-(4-toluoyl)-1*H*-benzimidazol-2-ylcarbamate.

[f] 1,3-Bis(5-benzoylbenzimidazol-2-yl)urea.

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 4 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

• **USP Reference Standards ⟨11⟩**

USP Mebendazole RS

USP Mebendazole Related Compound D RS

Methyl 5-benzoyl-1-methylbenzimidazol-2-ylcarbamate.

$C_{17}H_{15}N_3O_3$ 309.32

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
MEBENDAZOLE	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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