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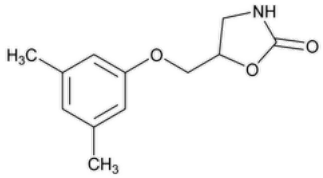
Metaxalone



$C_{12}H_{15}NO_3$ 221.25

2-Oxazolidinone, 5-[(3,5-dimethylphenoxy)methyl]-;

5-[(3,5-Xylyloxy)methyl]-2-oxazolidinone;

5-[(3,5-Dimethylphenoxy)methyl]-1,3-oxazolidin-2-one CAS RN®: 1665-48-1; UNII: 1NMA9J598Y.

DEFINITION

Metaxalone contains NLT 98.0% and NMT 102.0% of metaxalone ($C_{12}H_{15}NO_3$), calculated on dried basis.

IDENTIFICATION

Change to read:

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

Change to read:

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the ▲*Standard solution*,▲ (ERR 1-Apr-2019) as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: 0.68 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 4.5.

Mobile phase: Methanol and *Buffer* (50:50)

Standard stock solution: 0.5 mg/mL of USP Metaxalone RS prepared as follows. Transfer a suitable quantity of USP Metaxalone RS to a suitable volumetric flask. Add 50% of the flask volume of methanol. Sonicate for 5 min to dissolve. Add 40% of the flask volume of *Buffer*, and mix. Cool to room temperature. Dilute with *Buffer* to volume.

Standard solution: 0.05 mg/mL of USP Metaxalone RS from the *Standard stock solution* in *Mobile phase*

Sample stock solution: 0.5 mg/mL of Metaxalone prepared as follows. Transfer a suitable quantity of Metaxalone to a suitable volumetric flask. Add 50% of the flask volume of methanol. Sonicate for 5 min to dissolve. Add 40% of the flask volume of *Buffer*, and mix. Cool to room temperature. Dilute with *Buffer* to volume.

Sample solution: 0.05 mg/mL of Metaxalone from the *Sample stock solution* in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of metaxalone

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of metaxalone ($C_{12}H_{15}NO_3$) in the portion of Metaxalone taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.30%

• **Organic Impurities, Procedure 1**

If metaxalone related compound B, metaxalone related compound C, or *N*-benzyl metaxalone is a known process impurity, *Organic Impurities, Procedure 2* is recommended.

Solution A: 0.1% Trifluoroacetic acid in water

Solution B: 0.1% Trifluoroacetic acid in acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	75	25
10.0	65	35
11.0	75	25
15.0	75	25

Diluent: Acetonitrile and water (75:25)

System suitability solution: 4 mg/mL of USP Metaxalone RS and 0.01 mg/mL of 3,5-dimethylphenol in *Diluent*

Sensitivity solution: 0.002 mg/mL of USP Metaxalone RS in *Diluent*

Sample solution: 4 mg/mL of Metaxalone in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 273 nm

Column: 4.6-mm × 25-cm; 5-µm packing L68

Flow rate: 2.0 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Sensitivity solution*

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between metaxalone and 3,5-dimethylphenol, *System suitability solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Sample: *Sample solution*

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

$$\text{Result} = (r_U/r_T) \times 100$$

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

r_T = sum of the peak responses of metaxalone and impurities from the *Sample solution*

Acceptance criteria: See *Table 2*. Disregard any impurity peaks less than 0.03%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Metaxalone	1.0	—
3,5-Dimethylphenol	1.1	0.05
Any individual unspecified impurity	—	0.05
Total impurities	—	0.50

• **Organic Impurities, Procedure 2**

If metaxalone related compound B, metaxalone related compound C, or *N*-benzyl metaxalone is a known process impurity, *Organic Impurities, Procedure 2* is recommended. If the article complies with *Procedure 2*, the labeling indicates that it meets *Organic Impurities, Procedure 2*.

Buffer, Mobile phase, and **Standard stock solution:** Proceed as directed in the *Assay*.

Standard solution: 0.001 mg/mL of USP Metaxalone RS from the *Standard stock solution* in *Mobile phase*

Impurity stock solution: 0.2 mg/mL each of USP Metaxalone Related Compound B RS and USP Metaxalone Related Compound C RS in methanol. Sonicate to dissolve if necessary.

Peak identification solution: 1 mg/mL of USP Metaxalone RS and 0.02 mg/mL each of USP Metaxalone Related Compound B RS and USP Metaxalone Related Compound C RS prepared as follows. Transfer a suitable quantity of USP Metaxalone RS to a suitable volumetric flask. Add 50% of the flask volume of methanol, and sonicate to dissolve. Transfer suitable volumes of *Impurity stock solution* to the flask. Dilute with *Buffer* to volume.

Sample solution: 2.0 mg/mL of Metaxalone prepared as follows. Transfer a suitable quantity of Metaxalone to a suitable volumetric flask. Add 50% of the flask volume of methanol. Sonicate for 5 min to dissolve. Add 40% of the flask volume of *Buffer*, and mix. Cool to room temperature. Dilute with *Buffer* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 8 times the retention time of metaxalone

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 10.0%

Signal-to-noise ratio: NLT 25

Analysis

Samples: *Standard solution* and *Sample solution*

Use the *Peak identification solution* to identify the peaks.

Calculate the percentage of each impurity in the portion of Metaxalone 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 metaxalone from the *Standard solution*

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

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

F = relative response factor for the corresponding impurity (see *Table 3*)

Acceptance criteria: See *Table 3*. Disregard any impurity peaks less than 0.03%.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Metaxalone related compound B	0.35	1.0	0.05
Metaxalone	1.0	—	—
Metaxalone related compound C	3.6	1.0	0.05
N-Benzylmetaxalone[a]	6.9	0.64	0.05
Any individual unspecified impurity	—	1.0	0.05
Total impurities	—	—	0.3

[a] 3-Benzyl-5-[(3,5-dimethylphenoxy)methyl]oxazolidin-2-one.

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 90° for 2 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **Labeling:** The label states with which *Organic Impurities* procedure the article complies if *Organic Impurities, Procedure 1* is not used.

• **USP Reference Standards ⟨11⟩**

USP Metaxalone RS

USP Metaxalone Related Compound B RS

1-Amino-3-(3,5-dimethylphenoxy)propan-2-ol.

$C_{11}H_{17}NO_2$ 195.26

USP Metaxalone Related Compound C RS

Bis[2-hydroxy-3-(3,5-dimethylphenoxy)propyl]amine.

$C_{22}H_{31}NO_4$ 373.49

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

Topic/Question	Contact	Expert Committee
METAXALONE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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