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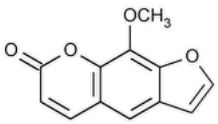
Methoxsalen



$C_{12}H_8O_4$ 216.19

7*H*-Furo[3,2-*g*][1]benzopyran-7-one, 9-methoxy-;

9-Methoxy-7*H*-furo[3,2-*g*][1]benzopyran-7-one;

9-Methoxy-7*H*-furo[3,2-*g*]chromen-7-one CAS RN®: 298-81-7.

DEFINITION

Methoxsalen contains NLT 98.0% and NMT 102.0% of methoxsalen ($C_{12}H_8O_4$), calculated on the anhydrous basis.

[**Caution—**Avoid contact with the skin.]

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 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**

Mobile phase: Acetonitrile and water (35:65)

Standard stock solution: 0.2 mg/mL of USP Methoxsalen RS in alcohol

Standard solution: 4 µg/mL of USP Methoxsalen RS in *Mobile phase* from the *Standard stock solution*

Sample stock solution: 0.2 mg/mL of Methoxsalen in alcohol

Sample solution: 4 µg/mL of Methoxsalen in *Mobile phase* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4-mm × 30-cm; packing L1; or 3.9-mm × 30-cm; 10-µm packing L1; or 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

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 methoxsalen ($C_{12}H_8O_4$) in the portion of Methoxsalen taken:

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

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

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

C_S = concentration of USP Methoxsalen RS in the *Standard solution* (µg/mL)

C_U = concentration of Methoxsalen in the *Sample solution* (µg/mL)

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

IMPURITIES

- **Residue on Ignition ⟨281⟩**

Sample: 1 g

Acceptance criteria: NMT 0.1%

- **Organic Impurities**

Solution A: 6% tetrahydrofuran in water

Solution B: Methanol

Solution C: *Solution A* and methanol (60:40)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)	Solution C (%)
0	0	0	100
21.00	0	0	100
21.01	60	40	0
40.00	35	65	0
45.00	60	40	0
45.01	0	0	100
50.00	0	0	100

Diluent: Acetonitrile and water (1:1)

System suitability solution: 0.05 mg/mL each of USP Methoxsalen Related Compound A RS and USP Methoxsalen Related Compound B RS in *Diluent*

Standard stock solution: 1.0 mg/mL of USP Methoxsalen RS in *Diluent*

Standard solution: 1.0 µg/mL of USP Methoxsalen RS in *Diluent* from the *Standard stock solution*

Sensitivity solution: 0.5 µg/mL of USP Methoxsalen RS in *Diluent* from the *Standard solution*

Sample solution: 1.0 mg/mL of Methoxsalen in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 247 nm

Column: 4.6-mm × 25-cm; 5-µm packing L11

Flow rate: 1.2 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.0 between methoxsalen related compound A and methoxsalen related compound B, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

r_S = peak area of methoxsalen from the *Standard solution*

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

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

F = relative response factor for each individual impurity (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Methoxsalen	1.00	1.0	—
Methoxsalen related compound B	1.50	0.51	0.15
Methoxsalen related compound A	1.57	0.68	0.15
Any individual unspecified impurity	—	—	0.10
Total impurities	—	—	0.5

SPECIFIC TESTS

• **Water Determination** ⟨921⟩, *Method I*: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers. Store at room temperature.

• **USP Reference Standards** ⟨11⟩

USP Methoxsalen RS

USP Methoxsalen Related Compound A RS

4-Methoxy-7*H*-furo[3,2-*g*]chromen-7-one.

$C_{12}H_8O_4$ 216.19

USP Methoxsalen Related Compound B RS

4,9-Dimethoxy-7*H*-furo[3,2-*g*]chromen-7-one.

$C_{13}H_{10}O_5$ 246.22

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

Topic/Question	Contact	Expert Committee
METHOXSALEN	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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