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Codeine Sulfate Oral Solution

DEFINITION
Codeine Sulfate Oral Solution contains NLT 93.0% and NMT 105.0% of the labeled amount of codeine sulfate $[(C_{18}H_{21}NO_3)_2 \cdot H_2SO_4]$.

IDENTIFICATION

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

• **B. Thin-Layer Chromatography**

Diluent: Methanol and water (25:75)

Standard solution: 1 mg/mL of USP Codeine Sulfate RS in *Diluent*

Sample solution: 1 mg/mL of codeine sulfate in *Diluent*

Chromatographic system

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: Methanol, ethyl acetate, water, and ammonium hydroxide (135: 85: 1: 0.5)

Analysis

Samples: *Standard solution* and *Sample solution*

Develop the plate until the solvent front has moved about three-fourths of the length of the plate, remove it, mark the solvent front, and allow the solvent to evaporate. Place the plate in an iodine chamber, and visualize it for NLT 5 min.

Acceptance criteria: The principal spot from the *Sample solution* corresponds in R_F value to that from the *Standard solution*.

ASSAY

• **Procedure**

[Note—Solutions are stable for 4 days at room temperature when stored in amber glassware.]

Buffer: 0.02 M ammonium acetate. Dissolve 1.54 g of ammonium acetate in 1 L of water, and adjust with glacial acetic acid to a pH of 4.2 ± 0.1.

Solution A: Dissolve 1.71 g of sodium decanesulfonic acid in 1 L of methanol and *Buffer* mixture (33:67). Pass through a filter of 0.45-µm pore size.

Solution B: Dissolve 1.71 g of sodium decanesulfonic acid in 1 L of methanol and *Buffer* mixture (63:37). Pass through a filter of 0.45-µm pore size.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
3.3	60	40
20	0	100
21	0	100
22	100	0

Time (min)	Solution A (%)	Solution B (%)
28	100	0

Diluent: Methanol and water (25:75)

Standard solution: 1.2 mg/mL of USP Codeine Sulfate RS in *Diluent*. Prepare by adding 70% of the flask volume of *Diluent*, and sonicate to dissolve. Dilute with *Diluent* to volume.

Sample solution: 1.2 mg/mL of codeine sulfate in *Diluent*, prepared by adding 70% of the flask volume of *Diluent*, then swirling, and letting it sit for 10 min. Dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Column temperature: 40 ± 2°

Flow rate: 1.2 mL/min

Injection volume: 30 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of codeine sulfate $[(C_{18}H_{21}NO_3)_2 \cdot H_2SO_4]$ in each mL of Oral Solution 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 Codeine Sulfate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of codeine sulfate in the *Sample solution* (mg/mL)

Acceptance criteria: 93.0%–105.0%

IMPURITIES

• **Organic Impurities**

Buffer, Solution A, Solution B, Mobile phase, Diluent, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Sensitivity solution: 0.6 µg/mL of USP Codeine Sulfate RS in *Diluent* from the *Standard solution*

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Relative standard deviation: NMT 2.0%, *Standard solution*

Tailing factor: NMT 2.0, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Oral Solution taken:

$$(r_U/r_S) \times (C_S/C_U) \times 100$$

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

r_S = response of codeine sulfate in the *Standard solution*

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

C_U = nominal concentration of codeine sulfate in the *Sample solution* (mg/mL)

Acceptance criteria

Individual impurities: See *Table 2*. Disregard any peak less than 0.05%.

Table 2

Related Compound	Relative Retention Time	Acceptance Criteria, NMT (%)
Codeine-*N*-oxide[a]	0.65	0.15
Codeine	1.00	—
Codeinone[b]	1.16	0.15
Individual unspecified degradant	—	0.15
Total impurities	—	0.5

[a] 7,8-Didehydro-4,5α-epoxy-3-methoxy-17-methylmorphinan-6α-ol *N*-oxide.

[b] 7,8-Didehydro-4,5α-epoxy-3-methoxy-17-methylmorphinan-6α-one.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 10^2 cfu/mL. The total yeasts and molds count does not exceed 20 cfu/mL. It meets the requirements of the test for absence of *Escherichia coli*.

• **pH ⟨791⟩:** 2.8–3.8

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Store at controlled room temperature in a well-sealed container.

• **USP Reference Standards ⟨11⟩**
USP Codeine Sulfate RS

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

Topic/Question	Contact	Expert Committee
CODEINE SULFATE ORAL SOLUTION	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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