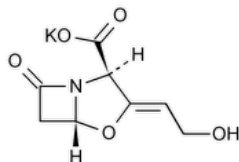


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Clavulanate Potassium



$C_8H_8KNO_5$ 237.25

4-Oxa-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 3-(2-hydroxyethylidene)-7-oxo-, monopotassium salt, 2*R*-(2 α ,3*Z*,5 α)-;

Potassium (Z)-(2*R*,5*R*)-3-(2-hydroxyethylidene)-7-oxo-4-oxa-1-azabicyclo[3.2.0]heptane-2-carboxylate CAS RN[®]: 61177-45-5; UNII: Q42OMW3AT8.

DEFINITION

Clavulanate Potassium contains the equivalent of NLT 75.5% and NMT 92.0% of clavulanic acid ($C_8H_8NO_5$), calculated on the anhydrous basis.

IDENTIFICATION

- **A.** The retention time of the major peak for clavulanic acid of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **B.** [IDENTIFICATION TESTS—GENERAL \(191\)](#), [Chemical Identification Tests, Potassium](#): Meets the requirements

ASSAY

PROCEDURE

Solution A: 7.8 mg/mL of [monobasic sodium phosphate](#) in [water](#). Adjust with [phosphoric acid](#) or [10 N sodium hydroxide](#) to a pH of 4.4 ± 0.1 before final dilution.

Mobile phase: [Methanol](#) and *Solution A* (1:19)

Standard solution: 0.25 mg/mL of [USP Clavulanate Lithium RS](#) in [water](#)

System suitability solution: 0.5 mg/mL of amoxicillin dissolved in *Standard solution*

Sample solution: 0.25 mg/mL of Clavulanate Potassium in [water](#)

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 220 nm

Column: 4-mm $\times$ 30-cm; 3- to 10- μ m packing [L1](#)

Flow rate: 2 mL/min

Injection volume: 20 μ L

System suitability

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

[NOTE—The relative retention times for clavulanic acid and amoxicillin are about 0.5 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.5 between the amoxicillin and clavulanic acid peaks, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of clavulanic acid ($C_8H_8NO_5$) in each mg of Clavulanate Potassium taken:

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



r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Clavulanate Lithium RS](#) in the *Standard solution* (mg/mL)

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

P = designated potency of [USP Clavulanate Lithium RS](#), in µg/mg of clavulanic acid

F = unit conversion factor, 0.001 mg/µg

Acceptance criteria: 75.5%–92.0% on the anhydrous basis

IMPURITIES

• PROCEDURE 1

Solution A: [0.05 M monobasic sodium phosphate](#). Adjust with [phosphoric acid](#) to a pH of 4.0 ± 0.1 .

Solution B: [Methanol](#) and *Solution A* (1:1)

System suitability solution: 0.1 mg/mL each of [USP Clavulanate Lithium RS](#) and amoxicillin in *Solution A*

Mobile phase: See [Table 1](#).

[NOTE—The system is equilibrated for 15 min with 100% *Solution A*.]

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
4	100	0
15	50	50
18	50	50
24	100	0

Standard solution: 0.1 mg/mL of [USP Clavulanate Lithium RS](#) in *Solution A*

Sample solution: 10.0 mg/mL of Clavulanate Potassium in *Solution A*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 10-cm; 5-µm packing [L1](#)

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

[NOTE—The relative retention times for clavulanic acid and amoxicillin are about 1.0 and 2.5, respectively.]

Suitability requirements

Resolution: NLT 13 between the clavulanic acid and amoxicillin peaks, *System suitability solution*

Tailing factor: NMT 2.0 for the clavulanic acid peak, *System suitability solution*

Relative standard deviation: NMT 2%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the Clavulanate Potassium taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$