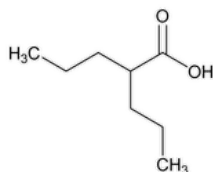


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Valproic Acid



$C_8H_{16}O_2$ 144.21

Pentanoic acid, 2-propyl-;

Propylvaleric acid CAS RN[®]: 99-66-1; UNII: 614OI1Z5WI.

DEFINITION

Valproic Acid contains NLT 98.0% and NMT 102.0% of valproic acid ($C_8H_{16}O_2$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197F
- **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

Buffer: 3.5 g/L of [monobasic sodium phosphate](#) in water. Adjust with [phosphoric acid](#) to a pH of 3.5.

Mobile phase: [Acetonitrile](#) and *Buffer* (45:55)

Diluent: [Acetonitrile](#) and water (45:55)

System suitability solution: 0.05 mg/mL of [USP Valproic Acid Related Compound B RS](#) and 0.5 mg/mL of [USP Valproic Acid RS](#) in *Diluent*

Standard solution: 0.5 mg/mL of [USP Valproic Acid RS](#) in *Diluent*

Sample solution: 0.5 mg/mL of Valproic Acid in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 15-cm; 5-μm packing [L7](#)

Flow rate: 1 mL/min

Injection volume: 20 μL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between valproic acid related compound B and valproic acid, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of valproic acid ($C_8H_{16}O_2$) in the portion of Valproic Acid taken:

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

r_U = peak response of valproic acid from the *Sample solution*

r_s = peak response of valproic acid from the *Standard solution*

C_s = concentration of [USP Valproic Acid RS](#) in the *Standard solution* (mg/mL)

C_u = concentration of Valproic Acid in the *Sample solution* (mg/mL)

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

IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

Change to read:

- **ORGANIC IMPURITIES**

▲ **System suitability solution:** 0.5 mg/mL of [USP Valproic Acid RS](#), 0.05 mg/mL of [USP Valproic Acid Related Compound B RS](#), and 0.05 mg/mL of [USP Valproic Acid Related Compound K RS](#) in [n-heptane](#)

Standard solution: 0.005 mg/mL of [USP Valproic Acid RS](#) in [n-heptane](#)

Sensitivity solution: 0.0025 mg/mL of [USP Valproic Acid RS](#) from *Standard solution* in [n-heptane](#)

Sample solution: 5 mg/mL of Valproic Acid in [n-heptane](#)

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 60-m capillary; coated with a 0.5-μm film of phase [G35](#)

Temperatures

Injection port: 220°

Detector: 220°

Column: See [Table 1](#).

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
100	0	100	5
100	4	200	15

Carrier gas: Helium

Flow rate: 2.0 mL/min

Injection volume: 2.0 μL

Injection type: Split, split ratio 5:1. [NOTE—Use of a split liner, deactivated with glass wool, is recommended.]

System suitability

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

[NOTE—The relative retention times for valproic acid related compound B, valproic acid, and valproic acid related compound A (also known as 2-allylpent-4-enoic acid) are about 0.97, 1.0, and 1.13, respectively. For other relative retention times, see [Table 2](#).]

Suitability requirements

Resolution: NLT 1.5 between valproic acid related compound B and valproic acid related compound K, *System suitability solution*

Tailing factor: NMT 1.5 for valproic acid, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Valproic Acid taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times (1/F) 100$$

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

r_s = peak response of valproic acid from the *Standard solution*

C_s = concentration of [USP Valproic Acid RS](#) in the *Standard solution* (mg/mL)

C_u = concentration of valproic acid in the *Sample solution* (mg/mL)

F = relative response factor (see [Table 2](#))

Acceptance criteria: See [Table 2](#). The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Valproic acid related compound K	0.98	0.89	0.15
Valproic acid	1.0	1.0	—
Any individual impurity	—	1.0	0.1
Total impurities	—	—	0.3▲ (USP 1-Aug-2022)

SPECIFIC TESTS

- [WATER DETERMINATION \(921\)](#), [Method I](#): NMT 1.0%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight glass, stainless steel, or polyethylene (HDPE) containers.

Change to read:

- [USP REFERENCE STANDARDS \(11\)](#).

[USP Valproic Acid RS](#)

▲ (USP 1-Aug-2022)
[USP Valproic Acid Related Compound B RS](#)
2-Isopropylpentanoic acid;
Also known as (2RS)-2-(1-Methylethyl)pentanoic acid.
 $C_8H_{16}O_2$ 144.21

▲ [USP Valproic Acid Related Compound K RS](#)
Ethylmethylvaleric acid;
Also known as 2-Ethyl-2-methylpentanoic acid.
 $C_8H_{16}O_2$ 144.21▲ (USP 1-Aug-2022)

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
VALPROIC ACID	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: [Chromatographic Database](#)

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