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Valproic Acid Capsules

DEFINITION
Valproic Acid Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of valproic acid ($C_8H_{16}O_2$).

IDENTIFICATION
- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectrum 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: 0.5 mg/mL of USP Valproic Acid RS and 50 µg/mL of USP Valproic Acid Related Compound B RS in *Diluent*

Standard solution: 0.5 mg/mL of USP Valproic Acid RS in *Diluent*

Sample solution: Nominally 0.5 mg/mL of valproic acid from the contents of the Capsules in *Diluent*, prepared as follows. Transfer a suitable portion of the contents of NLT 20 Capsules to an appropriate volumetric flask, and dilute with *Diluent* to volume. Sonicate the resulting solution for 5 min. Alternatively, stir the resulting solution for 1 h. Centrifuge a portion of the solution for about 10 min.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm. For *Identification* test *B*, use a diode array detector in the wavelength range of 200–300 nm.

Column: 4.6-mm × 15.0-cm; 5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for valproic acid related compound B and valproic acid are 0.90 and 1.0, respectively.]

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 the labeled amount of valproic acid ($C_8H_{16}O_2$) in the portion of Capsules 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 Valproic Acid RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Medium: 5 mg/mL of sodium lauryl sulfate in simulated intestinal fluid TS (prepared without the enzyme and with monobasic sodium phosphate instead of monobasic potassium phosphate), adjusted with 5 M sodium hydroxide to a pH of 7.5; 900 mL

Apparatus 2: 50 rpm

Time: 60 min

Buffer, Mobile phase, Diluent, System suitability solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Standard stock solution: 1.5 mg/mL of USP Valproic Acid RS in *Diluent*, prepared as follows. Transfer NLT 150 mg of USP Valproic Acid RS to a suitable volumetric flask. Add 10% of the flask volume of *Diluent* and dissolve the valproic acid. Dilute with *Diluent* to volume.

Standard solution: 0.3 mg/mL of USP Valproic Acid RS from the *Standard stock solution* and *Medium*

Sample solution: Pass a portion of the solution through suitable filter of 0.45-µm pore size and use the filtrate.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of valproic acid ($C_8H_{16}O_2$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

Tolerances: NLT 85% (Q) of valproic acid ($C_8H_{16}O_2$) is dissolved.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Valproic Acid RS

USP Valproic Acid Related Compound B RS

(2*RS*)-2-(1-Methylethyl)pentanoic acid.

$C_8H_{16}O_2$ 144.21

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

Topic/Question	Contact	Expert Committee
VALPROIC ACID CAPSULES	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

Most Recently Appeared In:
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