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Add the following:

▲Sodium Phenylbutyrate Oral Powder

DEFINITION
Sodium Phenylbutyrate Oral Powder contains NLT 90.0% and NMT 110.0% of the labeled amount of sodium phenylbutyrate ($C_{10}H_{11}NaO_2$).

IDENTIFICATION
- **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **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: Methanol, water, and glacial acetic acid (49:50:1)

Diluent: Methanol and water (20:80)

Standard solution: 2.5 mg/mL of USP Sodium Phenylbutyrate RS in *Diluent*. Sonicate, if necessary, to dissolve.

Sample solution: Nominally 2.5 mg/mL of sodium phenylbutyrate in *Diluent* prepared as follows. Transfer an amount of Oral Powder equivalent to about 500 mg of sodium phenylbutyrate to a 200-mL volumetric flask. Add about 140 mL of *Diluent*, and sonicate for 10 min with intermittent shaking. Dilute with *Diluent* to volume. Pass through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 260 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1.2 mL/min

Injection volume: 20 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 the labeled amount of sodium phenylbutyrate ($C_{10}H_{11}NaO_2$) in the portion of Oral Powder 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 Sodium Phenylbutyrate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of sodium phenylbutyrate in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS
- **Dissolution ⟨711⟩**

Medium: Simulated intestinal fluid without enzyme; 900 mL

Apparatus 2: 75 rpm

Time: 30 min

Mobile phase: Methanol, water, and glacial acetic acid (49:50:1)

Standard solution: (*L*/900) mg/mL of USP Sodium Phenylbutyrate RS, where *L* is the label claim of sodium phenylbutyrate in milligrams for each dosage strength prepared as follows. Transfer the appropriate amount of USP Sodium Phenylbutyrate RS to a volumetric flask. Add 40% of the final volume of methanol, and sonicate, if necessary, to dissolve. Dilute with *Medium* to volume.

Sample solution: Transfer carefully an amount of Oral Powder equivalent to each dosage strength, based on the label claim, to the dissolution vessel containing the *Medium*. Perform the dissolution test and pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 245 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1.7 mL/min

Injection volume: 10 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 the labeled amount of sodium phenylbutyrate ($C_{10}H_{11}NaO_2$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

L = label claim (mg/dosage strength)

V = volume of *Medium*, 900 mL

Tolerances: NLT 85% (*Q*) of the labeled amount of sodium phenylbutyrate ($C_{10}H_{11}NaO_2$) is dissolved.

- **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements

IMPURITIES

- **Organic Impurities**

Mobile phase: Methanol, water, and glacial acetic acid (44:55:1)

Diluent: Methanol and water (20:80)

System suitability stock solution A: 0.08 mg/mL of USP Phenylbutyrate Related Compound A RS in *Diluent*. Sonicate to dissolve, if necessary.

System suitability stock solution B: 0.06 mg/mL of USP Phenylbutyrate Related Compound B RS in *Diluent*. Sonicate to dissolve, if necessary.

System suitability solution: 4 mg/mL of USP Sodium Phenylbutyrate RS, 0.008 mg/mL of USP Phenylbutyrate Related Compound A RS, and 0.006 mg/mL of USP Phenylbutyrate Related Compound B RS prepared as follows. Dissolve a suitable amount of USP Sodium Phenylbutyrate RS with 50% of the total flask volume of methanol and sonicate, if necessary, to dissolve. Add suitable volumes of *System suitability stock solution A* and *System suitability stock solution B* to the same flask and dilute with *Diluent* to volume.

Sensitivity solution: 1.5 µg/mL each of USP Phenylbutyrate Related Compound A RS and USP Phenylbutyrate Related Compound B RS from *System suitability stock solution A* and *System suitability stock solution B* in *Diluent*

Standard solution: 0.008 mg/mL of USP Phenylbutyrate Related Compound A RS and 0.006 mg/mL of USP Phenylbutyrate Related Compound B RS from *System suitability stock solution A* and *System suitability stock solution B* in *Diluent*

Sample solution: Nominally 4 mg/mL of sodium phenylbutyrate in *Diluent* prepared as follows. Transfer an amount of Oral Powder equivalent to about 200 mg of sodium phenylbutyrate to a 50-mL volumetric flask. Add about 35 mL of *Diluent* and sonicate for 10 min with intermittent shaking. Dilute with *Diluent* to volume. Pass through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 245 nm

Column: 2.1-mm × 10-cm; 1.7-µm packing L1

Column temperature: 35°

Flow rate: 0.2 mL/min

Injection volume: 2 µL

System suitability

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

Suitability requirements

Resolution: NLT 6.0 between the phenylbutyrate related compound B and phenylbutyrate peaks, *System suitability solution*

Relative standard deviation: NMT 5.0% for the phenylbutyrate related compound A and phenylbutyrate related compound B peaks, *Standard solution*

Signal-to-noise ratio: NLT 10 for the phenylbutyrate related compound A and phenylbutyrate related compound B peaks, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of phenylbutyrate related compound A or phenylbutyrate related compound B in the portion of Oral Powder taken:

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

r_U = peak response of phenylbutyrate related compound A or phenylbutyrate related compound B from the *Sample solution*

r_S = peak response of phenylbutyrate related compound A or phenylbutyrate related compound B from the *Standard solution*

C_S = concentration of USP Phenylbutyrate Related Compound A RS or USP Phenylbutyrate Related Compound B RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of sodium phenylbutyrate in the *Sample solution* (mg/mL)

Calculate the percentage of any individual unspecified impurity in the portion of Oral Powder taken:

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

r_U = peak response of any individual unspecified impurity from the *Sample solution*

r_S = peak response of phenylbutyrate related compound A from the *Standard solution*

C_S = concentration of USP Phenylbutyrate Related Compound A RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of sodium phenylbutyrate in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Phenylbutyrate related compound A	0.30	0.15
Phenylbutyrate related compound B	0.68	0.15
Sodium phenylbutyrate	1.0	—
Any individual unspecified impurity	—	0.10

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Total impurities	—	0.5

SPECIFIC TESTS

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

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

USP Sodium Phenylbutyrate RS

USP Phenylbutyrate Related Compound A RS

3-Benzoylpropionic acid;
4-Oxo-4-phenylbutanoic acid.
$C_{10}H_{10}O_3$ 178.18

USP Phenylbutyrate Related Compound B RS

α-Tetralone;
3,4-Dihydronaphthalen-1(2*H*)-one.
$C_{10}H_{10}O$ 146.19▲ (USP 1-May-2021)

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

Topic/Question	Contact	Expert Committee
SODIUM PHENYLBUTYRATE ORAL POWDER	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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