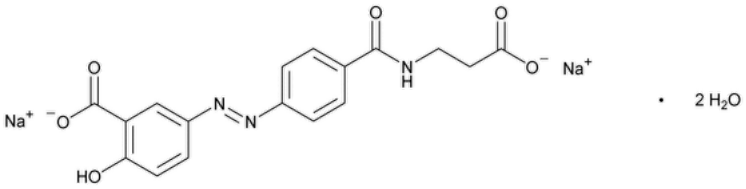
Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Dec-2024
Document Type: USP Monographs
DocId: GUID-FC685142-1B83-452E-BF30-B6B8A868B4A6_5_en-US
DOI: https://doi.org/10.31003/USPNF_M6988_05_01
DOI Ref: vo5oq

Balsalazide Disodium

Change to read:



$C_{17}H_{13}N_3Na_2O_6 \cdot 2H_2O$ ▲437.32▲ (CN 1-Dec-2024)

Benzoic acid, 5-[[4-[[(2-carboxyethyl)amino]carbonyl] phenyl]azo]-2-hydroxy-, disodium salt, dihydrate, (*E*)-;

(*E*)-5-[[*p*-[(2-Carboxyethyl)carbamoyl]phenyl]azo]salicylic acid, disodium salt, dihydrate CAS RN®: 150399-21-6; UNII: 1XL6BJI034.

DEFINITION

Balsalazide Disodium contains NLT 98.0% and NMT 102.0% of $C_{17}H_{13}N_3Na_2O_6 \cdot 2H_2O$, calculated on the as-is basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**
- **B. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**

  Sample solution: 10 µg/mL in water
- **C. Identification Tests—General, *Sodium*⟨191⟩**

ASSAY

- **Procedure**

  Sample: 219 mg

  Analysis: Add 80 mL of glacial acetic acid to the *Sample*, sonicate to dissolve, and titrate with 0.1 N perchloric acid VS. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N perchloric acid is equivalent to 21.87 mg of $C_{17}H_{13}N_3Na_2O_6 \cdot 2H_2O$.

  Acceptance criteria: 98.0%–102.0% on the as-is basis

IMPURITIES

Organic Impurities

[Note—On the basis of the synthetic route, perform either *Procedure 1* or *Procedure 2*. *Procedure 2* is recommended when impurities 1, 2, and 3 listed in *Impurity Table 2* may be present.]

- **Procedure 1**

  Solution A: Dissolve 2.7 g of monobasic potassium phosphate in 1000 mL of water, and adjust with 10% potassium hydroxide solution to a pH of 6.00±0.1.

  Diluent: Use *Solution A*.

  Solution B: Use acetonitrile.

  Standard solution: 0.5 µg/mL of USP Balsalazide Disodium RS, 0.5 µg/mL of USP Balsalazide Related Compound A RS, 0.5 µg/mL of USP Balsalazide Related Compound B RS, and 0.5 µg/mL of USP Salicylic Acid RS in *Diluent*. If needed, a small amount of acetonitrile may be added to facilitate dissolution. [Note—USP Balsalazide Related Compound A RS is the disodium salt of (*E*)-5-[(*p*-carboxyphenyl)azo]-2-salicylic acid. Use the correction factor stated on the label of the USP Reference Standard to calculate the concentration, as appropriate.]

  Sample solution: 1 mg/mL of Balsalazide Disodium in *Diluent*

  Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	90	10
4	90	10
40	75	25

Time (min)	Solution A (%)	Solution B (%)
47	75	25
55	50	50
60	50	50
60.1	90	10
70	90	10

Chromatographic system

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

Mode: LC

Detector: UV 238 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 45°

Flow rate: 1 mL/min

Injection size: 30 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 5 between balsalazide and balsalazide related compound B

Relative standard deviation: NMT 5% for each peak

Tailing factor: NMT 1.8 for the balsalazide peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Balsalazide Disodium taken:

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

r_U = peak response for each individual impurity from the *Sample solution*

r_S = peak response for the corresponding impurity from the *Standard solution*. [NOTE—For unspecified impurities, r_S is the peak response for the balsalazide peak from the *Standard solution*.]

C_S = concentration of the corresponding impurity in the *Standard solution* (mg/mL). [NOTE—For unspecified impurities, C_S is the concentration of balsalazide disodium in the *Standard solution*.]

C_U = concentration of Balsalazide Disodium in the *Sample solution* (mg/mL)

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Reporting level for impurities: 0.03%

Total impurities: NMT 1.0%

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Salicylic acid	0.37	0.05
Balsalazide related compound A[a]	0.70	0.05
Balsalazide	1.00	—
Balsalazide related compound B[b]	1.2	0.05

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Any other individual unspecified impurity	—	0.05

[a] (*E*)-5-[(*p*-Carboxyphenyl)azo]-2-salicylic acid.

[b] (*E*)-5-({*m*-[(2-Carboxyethyl)carbamoyl]phenyl}azo)-2-salicylic acid.

• **Procedure 2**

Solution A: Prepare 50 mM monobasic potassium phosphate buffer as follows: Dissolve 6.8 g of monobasic potassium phosphate in 1000 mL of water, and adjust with 2 N potassium hydroxide solution to a pH of 6.8–7.0. [Note—To ensure proper identification of impurity 1, the pH must be maintained between 6.8 and 7.0.]

Solution B: Acetonitrile, methanol and *Solution A* (5:1:14)

Solution C: Acetonitrile, methanol and *Solution A* (9:1:10)

Diluent: Use *Solution B*.

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)	Solution C (%)
0	100	0	0
37	0	100	0
60	0	0	100
75	100	0	0
85	100	0	0

Standard solution: 0.075 mg/mL of USP Balsalazide Disodium RS in *Diluent*. [Note—Use sonication to dissolve.]

Sensitivity solution: 0.375 µg/mL in *Diluent*, from *Standard solution*

System suitability solution: 1.5 mg/mL of USP Balsalazide Disodium RS and 1.5 µg/mL of USP Balsalazide Related Compound A RS in *Diluent*

Sample solution: 1.5 mg/mL of Balsalazide Disodium in *Diluent*. [Note—Use sonication to dissolve.]

Chromatographic system

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

Mode: LC

Detector: UV 300 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Column temperature: 25°–27°. [Note—To ensure proper identification of impurity 1, the column temperature must be maintained between 25° and 27°.]

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability

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

Suitability requirements

Resolution: NLT 8.5 between balsalazide related compound A and balsalazide, from the *System suitability solution*

Tailing factor: NMT 3.4 for the balsalazide peak, from the *System suitability solution*

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Balsalazide Disodium taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response for each individual impurity from the *Sample solution*

r_S = peak response for balsalazide from the *Standard solution*

C_S = concentration of USP Balsalazide Disodium RS in the *Standard solution*

C_U = concentration of Balsalazide Disodium in the *Sample solution* (mg/mL)

F = relative response factor (see *Impurity Table 2*)

Acceptance criteria

Individual impurities: See *Impurity Table 2*.

Reporting level for impurities: 0.03%

Total impurities: NMT 0.50%

Impurity Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
N-(4-Aminobenzoyl)-β-alanine[a]	0.29	1.8	0.05
Salicylic acid	0.55	1.4	0.05
Balsalazide related compound A[b]	0.88	1.4	0.05
Impurity 1[c]	0.91	1.9	0.05
Impurity 2[d]	0.92	1.4	0.05
Impurity 3[e]	0.94	0.83	0.05
Balsalazide	1.00		—
Impurity 4[f]	1.35	2.1	0.05
Impurity 5[g]	1.77	0.91	0.05
Any other individual unspecified impurity	—	—	0.05

[a] This impurity may be present as two peaks. Use the sum of the two peaks to determine compliance.

[b] (*E*)-5-[(*p*-Carboxyphenyl)azo]-2-salicylic acid.

[c] (*E,E*)-3,5-di-[4-(2-Carboxyethylcarbamoyl) phenylazo]-salicylic acid.

[d] (*E*)-3-[4-(2-Carboxyethylcarbamoyl) phenylazo]-salicylic acid.

[e] (*E,E*)-5-{{2-[4-(2-Carboxyethylcarbamoyl)phenylazo]-4-[2-carboxyethyl-carbamoyl]}phenylazo}-salicylic acid.

[f] (*E*)-2-[4-(2-Carboxyethylcarbamoyl)phenoxy]-5-{[4-(2-carboxyethyl-carbamoyl)]phenylazo}-benzoic acid

[g] (*E*)-2-Hydroxy-5-[[4-[[(3-isopropoxy-3-oxopropyl)amino]carbonyl] phenyl]azo]benzoic acid

SPECIFIC TESTS

• **Water Determination,** *Method Ia*⟨921⟩**:** 7.8%–9.0%

ADDITIONAL REQUIREMENTS

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

• **Labeling:** If a test for *Organic Impurities* other than *Test 1* is used, the labeling states the test with which the article complies.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Balsalazide Disodium RS

USP Balsalazide Related Compound A RS

(*E*)-5-[(*p*-Carboxyphenyl)azo]-2-salicylic acid, disodium salt.

$C_{14}H_8N_2O_5Na_2$ ▲330.21▲ (CN 1-Dec-2024)

USP Balsalazide Related Compound B RS

(*E*)-5-({*m*-[(2-Carboxyethyl)carbamoyl]phenyl}azo)-2-salicylic acid.

$C_{17}H_{15}N_3O_6$ ▲357.32▲ (CN 1-Dec-2024)

USP Salicylic Acid RS

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

Topic/Question	Contact	Expert Committee
BALSALAZIDE DISODIUM	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 35(4)

Current DocID: GUID-FC685142-1B83-452E-BF30-B6B8A868B4A6_5_en-US

DOI: https://doi.org/10.31003/USPNF_M6988_05_01

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