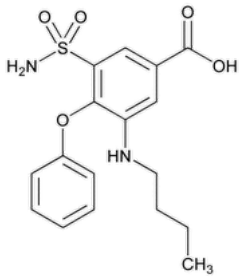
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2024
Document Type: USP Monographs
DocId: GUID-5CDA85B9-9D2F-455E-83EC-194762A61EDC_5_en-US
DOI: https://doi.org/10.31003/USPNF_M10463_05_01
DOI Ref: 8v2nm

Bumetanide



$C_{17}H_{20}N_2O_5S$ 364.42

Benzoic acid, 3-(aminosulfonyl)-5-(butylamino)-4-phenoxy-;

3-(Butylamino)-4-phenoxy-5-sulfamoylbenzoic acid CAS RN®: 28395-03-1; UNII: 0Y2S3XUQ5H.

DEFINITION

Bumetanide contains NLT 98.0% and NMT 102.0% of bumetanide ($C_{17}H_{20}N_2O_5S$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197M ▲or 197A▲ (USP 1-May-2024)

Change to read:

• **B.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2024)

Delete the following:

▲• **C.**▲ (USP 1-May-2024)

ASSAY

Change to read:

• **Procedure**

▲**Solution A:** 0.5% (v/v) formic acid in water prepared as follows. To a 1-L volumetric flask, add 5 mL of formic acid and dilute with water to volume.

Solution B: Methanol

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	60	40
2	60	40
10	20	80
15	20	80
15.1	60	40
20	60	40

Standard stock solution: 0.2 mg/mL of USP Bumetanide RS in methanol

Standard solution: 0.1 mg/mL of USP Bumetanide RS from the *Standard stock solution* in water

Sample stock solution: 0.2 mg/mL of Bumetanide in methanol

Sample solution: 0.1 mg/mL of Bumetanide from the *Sample stock solution* in water

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of bumetanide ($C_{17}H_{20}N_2O_5S$) in the portion of Bumetanide taken:

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

r_U = peak response of bumetanide from the *Sample solution*

r_S = peak response of bumetanide from the *Standard solution*

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

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

▲ (USP 1-May-2024)

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

IMPURITIES

Change to read:

• **Residue on Ignition ⟨281⟩:** NMT 0.1%▲▲ (USP 1-May-2024)

Change to read:

• **Organic Impurities**

▲**Solution A, Solution B,** and **Mobile phase:** Prepare as directed in the *Assay*.

Diluent: Methanol and water (40:60)

Standard stock solutions: 0.1 mg/mL each of USP Bumetanide RS, USP Bumetanide Related Compound A RS, USP Bumetanide Related Compound B RS, and 0.005 mg/mL of USP Butyl 3-(butylamino)-4-phenoxy-5-sulfamoylbenzoate RS individually prepared as follows. Transfer suitable amounts each of USP Bumetanide RS, USP Bumetanide Related Compound A RS, USP Bumetanide Related Compound B RS, and USP Butyl 3-(butylamino)-4-phenoxy-5-sulfamoylbenzoate RS to separate suitable volumetric flasks. Add methanol to about 40% of the total volume of each flask to dissolve the solids. Dilute with water to volume.

Standard solution: 0.2 µg/mL each of USP Bumetanide RS, USP Bumetanide Related Compound A RS, USP Bumetanide Related Compound B RS, and USP Butyl 3-(butylamino)-4-phenoxy-5-sulfamoylbenzoate RS from the corresponding *Standard stock solutions* in *Diluent*

Sensitivity solution: 0.125 µg/mL each of USP Bumetanide RS, USP Bumetanide Related Compound A RS, USP Bumetanide Related Compound B RS, and USP Butyl 3-(butylamino)-4-phenoxy-5-sulfamoylbenzoate RS from the corresponding *Standard stock solutions* in *Diluent*

Sample solution: 0.2 mg/mL of Bumetanide prepared as follows. To a suitable amount of Bumetanide in a suitable volumetric flask, add methanol to about 40% of the total volume to dissolve the solids. Dilute with water to volume.

Chromatographic system: Proceed as directed in the *Assay*, except for the *Injection volume*.

Injection volume: 50 µL

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

[Note—See *Table 2* for the relative retention times.]

Resolution: NLT 20 between bumetanide related compound A and bumetanide related compound B, *Standard solution*

Relative standard deviation: NMT 5.0% for each peak, *Standard solution*

Signal-to-noise ratio: NLT 10 for each peak, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each specified impurity in the portion of Bumetanide taken:

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

r_U = peak response of each specified impurity from the *Sample solution*

r_S = peak response of the corresponding bumetanide related compound from the *Standard solution*

C_S = concentration of the corresponding bumetanide related compound Reference Standard in the *Standard solution* (mg/mL)

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

Calculate the percentage of any unspecified impurity in the portion of Bumetanide taken:

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

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

r_S = peak response of bumetanide from the *Standard solution*

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

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

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Bumetanide related compound A	0.3	0.1
Bumetanide related compound B	0.7	0.2
Bumetanide	1.0	—
Butyl 3-(butylamino)-4-phenoxy-5-sulfamoylbenzoate	1.4	0.1
Any unspecified impurity	—	0.10
Total impurities[a]	—	0.4

[a] Bumetanide related compound A, bumetanide related compound B, and butyl 3-(butylamino)-4-phenoxy-5-sulfamoylbenzoate are not included.

▲ (USP 1-May-2024)

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Sample: Dry at 105° for 4 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

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

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Bumetanide RS

USP Bumetanide Related Compound A RS

3-Amino-4-phenoxy-5-sulfamoylbenzoic acid.

$C_{13}H_{12}N_2O_5S$ 308.31

USP Bumetanide Related Compound B RS

3-Nitro-4-phenoxy-5-sulfamoylbenzoic acid.

$C_{13}H_{10}N_2O_7S$ 338.29

USP Butyl 3-(butylamino)-4-phenoxy-5-sulfamoylbenzoate RS $C_{21}H_{28}N_2O_5S$ ▲420.52▲ (USP 1-May-2024)

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

Topic/Question	Contact	Expert Committee
BUMETANIDE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 47(4)

Current DocID: GUID-5CDA85B9-9D2F-455E-83EC-194762A61EDC_5_en-US

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