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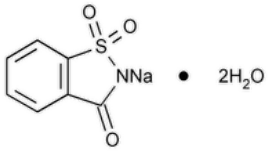
Saccharin Sodium



$C_7H_4NNaO_3S \cdot 2H_2O$ 241.20
$C_7H_4NNaO_3S$ 205.17
1,2-Benzisothiazol-3(2*H*)-one, 1,1-dioxide, sodium salt, dihydrate;
1,2-Benzisothiazolin-3-one 1,1-dioxide sodium salt dihydrate CAS RN®: 6155-57-3.
Anhydrous CAS RN®: 128-44-9.

DEFINITION

Saccharin Sodium contains NLT 98.0% and NMT 102.0% of saccharin sodium ($C_7H_4NNaO_3S$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

Sample: Dry at 105° to constant weight.

Acceptance criteria: Meets the requirements

• **B.**

Sample solution: 100 mg/mL

Potassium pyroantimonate solution: Dissolve 2 g of potassium pyroantimonate in 95 mL of hot water. Cool quickly, and add 50 mL of a potassium hydroxide solution (50 mg/mL) and 1 mL of sodium hydroxide solution (8.5 in 100). Allow to stand for 24 h, filter, and dilute with water to 150 mL.

Analysis: To 10 mL of the *Sample solution* add 2 mL of 15% potassium carbonate, and heat to boiling. No precipitate is formed. Add 4 mL of *Potassium pyroantimonate solution*, and heat to boiling. Allow to cool in ice water and, if necessary, rub the inside of the test tube with a glass rod.

Acceptance criteria: A dense precipitate is formed.

• **C.** Sodium salts impart an intense yellow color to a nonluminous flame.

ASSAY

• **Procedure**

Solution A: 50 mM dibasic potassium phosphate (K_2HPO_4) buffer in 0.1% (v/v) phosphoric acid solution

Solution B: Methanol

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
7.0	90	10

Time (min)	Solution A (%)	Solution B (%)
8.0	5	95
10.0	5	95
10.1	90	10
15.0	90	10

Diluent: Methanol and water (50:50 v/v)

System suitability solution: 0.1 mg/mL of phthalic anhydride and 0.1 mg/mL of USP Saccharin Sodium RS in *Diluent*

Standard solution: 0.1 mg/mL of USP Saccharin Sodium RS in *Diluent*

Sample solution: 0.1 mg/mL of Saccharin Sodium in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

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

Column temperature: 20 ± 5°

Flow rate: 1.0 mL/min

Injection volume: 10 µL

Run time: 15 min

System suitability

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

[NOTE—The retention times for phthalic anhydride and saccharin sodium are about 6.3 and 7.3 min, respectively. Phthalic anhydride is a potential impurity.]

Suitability requirements

Resolution: NLT 1.5 between the phthalic anhydride and saccharin sodium peaks, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 0.73% for five replicate injections, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of saccharin sodium in the portion of Saccharin Sodium taken:

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

r_U = peak area of saccharin sodium from the *Sample solution*

r_S = peak area of saccharin sodium from the *Standard solution*

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

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

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

IMPURITIES

• **LIMIT OF TOLUENESULFONAMIDES**

Internal standard solution: 0.25 mg/mL of caffeine in methylene chloride

Standard stock solution: 20.0 µg/mL of USP *o*-Toluenesulfonamide RS and 20.0 µg/mL of USP *p*-Toluenesulfonamide RS in methylene chloride

Standard solution: Evaporate 5.0 mL of *Standard stock solution* to dryness in a stream of nitrogen. Dissolve the residue in 1.0 mL of the *Internal standard solution*.

Sample stock solution: 200 mg/mL in water. If necessary, adjust with 1 N sodium hydroxide or 1 N hydrochloric acid to a pH of 7–8 before final dilution.

Sample solution: Shake 50 mL of the *Sample stock solution* with four quantities each of 50 mL of methylene chloride. Combine the lower layers, dry over anhydrous sodium sulfate, and filter. Wash the filter and the sodium sulfate with 10 mL of methylene chloride. Combine the solution and the washings, and evaporate almost to dryness in a water bath at a temperature not exceeding 40°. Using a small quantity of methylene chloride, quantitatively transfer the residue into a suitable 10-mL tube, evaporate to dryness in a stream of nitrogen, and dissolve the residue in 1.0 mL of the *Internal standard solution*.

Blank solution: Evaporate 200 mL of methylene chloride to dryness in a water bath at a temperature not exceeding 40°. Dissolve the residue in 1 mL of methylene chloride.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 10-m fused silica; coated with a 2-µm film of phase G3

Temperatures

Injection port: 250°

Column: 180°

Detector: 250°

Carrier gas: Nitrogen

Flow rate: 10 mL/min

Injection volume: 1 µL

Injection type: Split ratio, 2:1

System suitability

Samples: *Standard solution* and *Blank solution*

[Note—The substances are eluted in the following order: *o*-toluenesulfonamide, *p*-toluenesulfonamide, and caffeine.]

Suitability requirements: No peaks at the retention times for the internal standard, *o*-toluenesulfonamide, or *p*-toluenesulfonamide, *Blank solution*

Resolution: NLT 1.5 between *o*-toluenesulfonamide and *p*-toluenesulfonamide, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: See *Table 2*. If any peaks due to *o*-toluenesulfonamide and *p*-toluenesulfonamide appear in the chromatogram of the *Sample solution*, the ratio of their areas to that of caffeine (internal standard) is NMT the corresponding ratio in the chromatogram of the *Standard solution*.

Table 2

Name	Acceptance Criteria, NMT (ppm)
o-Toluenesulfonamide	10
p-Toluenesulfonamide	10

• **Limit of Benzoate and Salicylate**

Sample solution: 50 mg/mL

Analysis: To 10 mL of the *Sample solution* add 5 drops of 6 N acetic acid, and then add 3 drops of ferric chloride TS.

Acceptance criteria: No precipitate or violet color appears.

SPECIFIC TESTS

• **Water Determination ⟨921⟩, *Method I*:** NMT 15.0%

Change to read:

• **Readily Carbonizable Substances Test ⟨271⟩**

Matching fluid A: Cobaltous chloride CS, ferric chloride ▲CS,▲ (ERR 1-May-2020) cupric sulfate CS, and water (0.1:0.4:0.1:4.4)

Sample solution: 40 mg/mL in sulfuric acid maintained at 48°–50° for 10 min

Acceptance criteria: The *Sample solution* has no more color than *Matching fluid A*, when viewed against a white background.

• **Acidity or Alkalinity**

Sample solution: 100 mg/mL in carbon dioxide-free water

Analysis: To 10 mL of the *Sample solution* add 1 drop of phenolphthalein TS.

Acceptance criteria: No red or pink color is produced. Then add 1 drop of 0.1 N sodium hydroxide: a red or pink color is produced.

• **Clarity of Solution**

[Note—The *Sample solution* is to be compared to *Reference suspension A* in diffused daylight 5 min after preparation of *Reference suspension A*.]

Hydrazine solution: 10.0 mg/mL of hydrazine sulfate in water. [Note—Allow to stand for 4–6 h.]

Methenamine solution: Transfer 2.5 g of methenamine to a 100-mL glass-stoppered flask, add 25.0 mL of water, insert the glass stopper, and mix to dissolve.

Primary opalescent suspension: Transfer 25.0 mL of *Hydrazine solution* to the *Methenamine solution* in the 100-mL glass-stoppered flask. Mix, and allow to stand for 24 h. [Note—This suspension is stable for 2 months, provided it is stored in a glass container free from surface defects. The suspension must not adhere to the glass and must be well mixed before use.]

Opalescence standard: Transfer 15.0 mL of the *Primary opalescent suspension*, dilute with water to 1000 mL, and mix. [Note—This suspension should not be used beyond 24 h after preparation.]

Reference suspension A: *Opalescence standard* and water (1 in 20)

Reference suspension B: *Opalescence standard* and water (1 in 10)

Sample solution: 200 mg/mL in water

Analysis

Samples: *Reference suspension A*, *Reference suspension B*, *Sample solution*, and water

Transfer a sufficient portion of the *Sample solution* to a test tube of colorless, transparent, neutral glass with a flat base and an internal diameter of 15–25 mm to obtain a depth of 40 mm. Similarly transfer portions of *Reference suspension A*, *Reference suspension B*, and water to separate matching test tubes. Compare solutions in diffused daylight, viewing vertically against a black background (see *Visual Comparison* ⟨630⟩).

[Note—The diffusion of light must be such that *Reference suspension A* can readily be distinguished from water, and that *Reference suspension B* can readily be distinguished from *Reference suspension A*.]

Acceptance criteria: The *Sample solution* shows the same clarity as that of water, or its opalescence is NMT that of *Reference suspension A*.

• **Color of Solution**

Diluent: 10-g/L solution of hydrochloric acid

Standard stock solution: Ferric chloride CS, cobaltous chloride CS, cupric sulfate CS, and *Diluent* (3.0:3.0:2.4:1.6)

Standard solution: *Standard stock solution* and *Diluent* (1 in 100). [Note—Prepare the *Standard stock solution* and *Standard solution* immediately before use.]

Sample solution: Use the *Sample solution* from the test for *Clarity of Solution*.

Analysis

Samples: *Standard solution*, *Sample solution*, and water

Transfer a sufficient portion of the *Sample solution* to a test tube of colorless, transparent, neutral glass with a flat base and an internal diameter of 15–25 mm to obtain a depth of 40 mm. Similarly transfer portions of the *Standard solution* and water to separate, matching test tubes. Compare the solutions in diffused daylight, viewing vertically against a white background (see *Visual Comparison* ⟨630⟩).

Acceptance criteria: The *Sample solution* has the appearance of water or is not more intensely colored than the *Standard solution*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at room temperature.

• **Labeling:** Where the quantity of saccharin sodium is indicated in the labeling of any preparation containing Saccharin Sodium, this shall be expressed in terms of saccharin ($C_7H_5NO_3S$).

• **USP Reference Standards** ⟨11⟩

USP Saccharin Sodium RS

USP *o*-Toluenesulfonamide RS

USP *p*-Toluenesulfonamide RS

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

Topic/Question	Contact	Expert Committee
SACCHARIN SODIUM	Documentary Standards Support	SE2020 Simple Excipients
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

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