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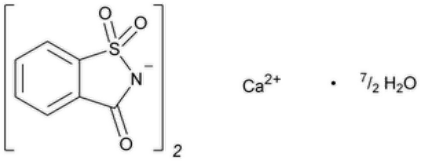
Saccharin Calcium



$C_{14}H_8CaN_2O_6S_2 \cdot 3½H_2O$ 467.48
$C_{14}H_8CaN_2O_6S_2$ 404.44
1,2-Benzisothiazol-3(2*H*)-one, 1,1-dioxide, calcium salt, hydrate (2:7);
1,2-Benzisothiazolin-3-one 1,1-dioxide calcium salt hydrate (2:7) CAS RN®: 6381-91-5.
Anhydrous CAS RN®: 6485-34-3.

DEFINITION

Change to read:

Saccharin Calcium contains ▲NLT 98.0% and NMT 102.0%▲ (USP 1-May-2020) of saccharin calcium ($C_{14}H_8CaN_2O_6S_2$), 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
Analysis: To the *Sample solution* add 2 drops of methyl red TS, and neutralize with 6 N ammonium hydroxide. Add 3 N hydrochloric acid, dropwise, until the solution is acid to the indicator. Add ammonium oxalate TS.
Acceptance criteria: A white precipitate is formed when the ammonium oxalate is added. This precipitate is insoluble in 6 N acetic acid but dissolves in hydrochloric acid.

• **C.** Calcium salts moistened with hydrochloric acid impart a transient yellowish-red color to a nonluminous flame.

ASSAY

Change to read:

• **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 Calcium RS in *Diluent*

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

Sample solution: 0.1 mg/mL of Saccharin Calcium 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 calcium 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 calcium 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 calcium in the portion of Saccharin Calcium taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the anhydrous basis▲ (USP 1-May-2020)

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

Injector: 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: There are no peaks present in the *Blank solution* at the retention times of the *Internal standard solution*, *o*-toluenesulfonamide, and *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 obtained with the *Sample solution*, the ratio of their areas to that of the *Internal standard solution* is NMT the corresponding ratio in the chromatogram obtained with 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 3 drops of ferric chloride TS.

Acceptance criteria: No precipitate or violet color appears.

SPECIFIC TESTS

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

Change to read:

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

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

Sample solution: 40 mg/mL in sulfuric acid▲maintained at▲ (USP 1-May-2020) 48°–50° for 10 min

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

• **Clarity of Solution**

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

Diluent: 200-g/L solution of sodium acetate

Hydrazine solution: 10.0 mg/mL of hydrazine sulfate. [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* and dilute to 1000 mL. [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 *Diluent*

Analysis

Samples: *Diluent*, *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*, water, and *Diluent* 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 *Diluent*, or its opalescence is NMT that of *Reference suspension A*.

Change to read:

• **COLOR OF SOLUTION**

Diluent A: 200-g/L solution of sodium acetate

Diluent B: 10-g/L solution of hydrochloric acid

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

Standard solution: *Standard stock solution* and *Diluent B* (1:99). [NOTE—Prepare the ▲*Standard stock solution* and▲ (USP 1-May-2020) *Standard solution* immediately before use.]

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

Analysis

Samples: *Diluent A*, *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*, *Diluent A*, and water to separate matching test tubes. Compare 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 *Diluent A*, 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 calcium is indicated in the labeling of any preparation containing Saccharin Calcium, this shall be expressed in terms of saccharin ($C_7H_5NO_3S$).

Change to read:

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Saccharin Calcium RS

USP *o*-Toluenesulfonamide RS ▲▲ (USP 1-May-2020)

USP *p*-Toluenesulfonamide RS ▲▲ (USP 1-May-2020)

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

Topic/Question	Contact	Expert Committee
SACCHARIN CALCIUM	Documentary Standards Support	SE2020 Simple Excipients

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

Chromatographic Database Information: Chromatographic Database

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