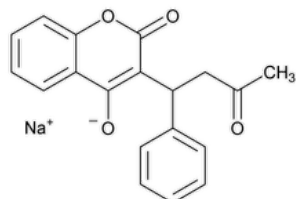


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Warfarin Sodium



$C_{19}H_{15}NaO_4$ 330.31

2*H*-1-Benzopyran-2-one, 4-hydroxy-3-(3-oxo-1-phenylbutyl)-, sodium salt;

3-(α -Acetonylbenzyl)-4-hydroxycoumarin sodium salt;

Sodium 2-oxo-3-(3-oxo-1-phenylbutyl)-2*H*-chromen-4-olate CAS RN®: 129-06-6; UNII: 6153CWM0CL.

DEFINITION

Warfarin Sodium is an amorphous solid or a crystalline clathrate. The crystalline form consists principally of warfarin sodium and isopropyl alcohol in a 2:1 molecular ratio. It contains NLT 8.0% and NMT 8.5% of isopropyl alcohol. Warfarin Sodium contains NLT 97.0% and NMT 102.0% of warfarin sodium ($C_{19}H_{15}NaO_4$), calculated on the anhydrous basis for the amorphous form or on the anhydrous and isopropyl alcohol-free basis for the crystalline form.

IDENTIFICATION

Change to read:

- **A.** ▲ **SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy: 197K** ▲ (CN 1-MAY-2020)

Standard: Use [USP Warfarin RS](#).

Sample: Dissolve 100 mg in 25 mL of [water](#), and adjust with [hydrochloric acid](#) to a pH of less than 3, using short-range pH indicator paper. Stir the mixture, and allow the precipitate to coagulate. Filter the mixture, wash the precipitate with four, 5-mL portions of [water](#), and dry under vacuum over [phosphorus pentoxide](#) for 4 h. Use the warfarin obtained.

- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

• **C.**

Methoxyphenylacetic reagent: Dissolve 2.7 g of [methoxyphenylacetic acid](#) in 6 mL of [10% tetramethylammonium hydroxide aqueous solution](#), and add 20 mL of absolute alcohol.

Diluted ammonia: Dilute 41 g of [ammonium hydroxide](#) with [water](#) to 100 mL.

Ammonium carbonate solution: 158 mg/mL of [ammonium carbonate](#) in [water](#)

Sample solution: Dissolve 30 mg of Warfarin Sodium in 0.5 mL of [water](#).

Analysis: Add 1.5 mL of *Methoxyphenylacetic reagent* to the *Sample solution*, and cool in ice water for 30 min.

Acceptance criteria: A voluminous, white, crystalline precipitate is formed. Place the precipitate in a water bath at 20° and stir for 5 min. The precipitate does not disappear. Add 1 mL of *Diluted ammonia*. The precipitate dissolves completely. Add 1 mL of *Ammonium carbonate solution*. No precipitate is formed.

ASSAY

• PROCEDURE

Buffer: Transfer 1.36 g of [monobasic potassium phosphate](#) to a 200-mL volumetric flask, and dissolve in 50 mL of [water](#). Add 39.1 mL of 0.2 N [sodium hydroxide](#), and dilute with [water](#) to volume. Adjust with [sodium hydroxide](#) or [phosphoric acid](#) to a pH of 7.4 ± 0.1.

Mobile phase: [Methanol](#), [glacial acetic acid](#), and [water](#) (64:1:36)

Standard stock solution: 0.376 mg/mL of [USP Warfarin RS](#) prepared as follows. Transfer [USP Warfarin RS](#) to a suitable volumetric flask, and dissolve in [0.1 N sodium hydroxide](#) equivalent to 39% of the final volume. Add 0.2 M [monobasic potassium phosphate](#), equivalent to 25% of the final volume, and dilute with [water](#) to volume.

Standard solution: Transfer 5 mL of *Standard stock solution* and 15 mL of *Buffer* into a conical flask, and mix.



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Sample stock solution: 0.4 mg/mL of Warfarin Sodium prepared as follows. Transfer 100 mg of Warfarin Sodium, accurately weighed, to a 250-mL volumetric flask, and dissolve in 97.8 mL of [0.1 N sodium hydroxide](#). Add 62.5 mL of 0.2 M [monobasic potassium phosphate](#), and dilute with [water](#) to volume.

Sample solution: Transfer 5 mL of *Sample stock solution* and 15 mL of *Buffer* into a conical flask, and mix.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; packing [L7](#)

Flow rate: 1.4 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of warfarin sodium ($C_{19}H_{15}NaO_4$) in the portion of Warfarin Sodium taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

C_S = concentration of [USP Warfarin RS](#) in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of warfarin sodium, 330.31

M_{r2} = molecular weight of warfarin, 308.33

Acceptance criteria: 97.0%–102.0% on the anhydrous basis for the amorphous form or on the anhydrous and isopropyl alcohol-free basis for the crystalline form

IMPURITIES

• ORGANIC IMPURITIES

Diluent: [Methanol](#) and [water](#) (25:75)

Mobile phase: [Acetonitrile](#), [glacial acetic acid](#), and [water](#) (32:1:68)

Standard stock solution: 0.12 mg/mL each of [USP Warfarin RS](#) and [USP Warfarin Related Compound A RS](#) prepared as follows. Transfer [USP Warfarin RS](#) and [USP Warfarin Related Compound A RS](#) to a suitable volumetric flask, and add [0.1 N sodium hydroxide](#) and [methanol](#) equivalent to 2% and 25% of the final volume, respectively. Dilute with [water](#) to volume.

Standard solution: 2.4 µg/mL each of [USP Warfarin RS](#) and [USP Warfarin Related Compound A RS](#) in *Diluent*, from *Standard stock solution*

Sample solution: 0.8 mg/mL of Warfarin Sodium in *Diluent*

System suitability solution: 2.4 µg/mL of [USP Warfarin Related Compound A RS](#) and 0.8 mg/mL of Warfarin Sodium in *Diluent* prepared as follows. Transfer 0.5 mL of *Standard stock solution* to a 25-mL volumetric flask and dilute with *Sample solution* to volume.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 260 nm

Column: 4.6-mm × 25-cm; packing [L10](#)

Column temperature: 35°

Flow rate: 1.5 mL/min

Injection volume: 50 µL

Run time: NLT 2 times the retention time of the warfarin peak

System suitability

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