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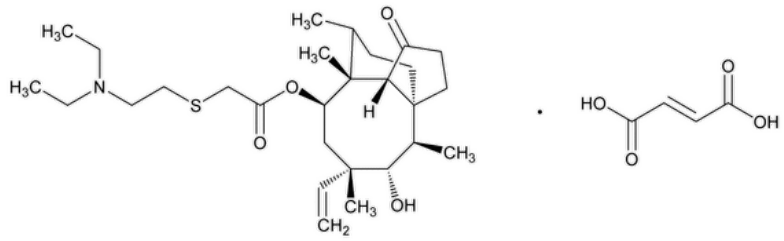
Tiamulin Fumarate



$C_{28}H_{47}NO_4S \cdot C_4H_4O_4$ 609.82

Tiamulin hydrogen fumarate;

Acetic acid, [[2-(diethylamino)ethyl]thio]-, 6-ethenyl-decahydro-5-hydroxy-4,6,9,10-tetramethyl-1-oxo-3a,9-propano-3a*H*-cyclopentacycloocten-8-yl ester [3a*S*-(3aα,4β,5α,6α,8β,9α,9aβ,10*S**)]-, (*E*)-2-butenedioate (1:1) (salt);

[[2-(Diethylamino)ethyl]thio]acetic acid 8-ester with (3a*S*,4*R*,5*S*,6*S*,8*R*,9*R*,9a*R*,10*R*)-octahydro-5,8-dihydroxy-4,6,9,10-tetramethyl-6-vinyl-3a,9-propano-3a*H*-cyclopentacycloocten-1(4*H*)-one fumarate (1:1) (salt) CAS RN®: 55297-96-6; UNII: ION1Q02ZCX.

DEFINITION

Tiamulin Fumarate contains NLT 97.0% and NMT 102.0% of tiamulin fumarate ($C_{28}H_{47}NO_4S \cdot C_4H_4O_4$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K[Note—When using 197K, intimately mix Tiamulin Fumarate with potassium bromide, but do not grind.]▲ (CN 1-May-2020)

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

ASSAY

• **Procedure**

Solution A: 6% perchloric acid

Buffer: Transfer 10 g of ammonium carbonate to a 1000-mL volumetric flask, and dissolve in 800 mL of water. Add 24 mL of *Solution A*, and dilute with water to volume.

Mobile phase: Methanol, acetonitrile, and *Buffer* (49:23:28)

System suitability solution: 0.08 mg/mL of USP Tiamulin Fumarate RS and 0.08 mg/mL of USP Tiamulin Related Compound A RS in *Mobile phase*

Standard solution: 4 mg/mL of USP Tiamulin Fumarate RS in *Mobile phase*

Sample solution: 4 mg/mL of Tiamulin Fumarate in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 212 nm

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

Column temperature: 30 ± 3°

Flow rate: 1.2 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

[Note—The tiamulin related compound A peak elutes before the tiamulin fumarate peak.]

Resolution: NLT 2.0 between tiamulin related compound A and tiamulin fumarate, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of tiamulin fumarate ($C_{28}H_{47}NO_4S \cdot C_4H_4O_4$) in the portion of Tiamulin Fumarate taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 97.0%–102.0% on the dried basis

OTHER COMPONENTS

• **Content of Fumarate**

Sample solution: 450 mg of Tiamulin Fumarate in 60 mL of a mixture of alcohol and water (1:1)

Analysis: Titrate the *Sample solution* with 0.1 N sodium hydroxide VS, using a glass–calomel electrode (see *Titrimetry* ⟨541⟩). Perform a blank determination, and make any necessary correction. Each milliliter of 0.1 N sodium hydroxide is equivalent to 5.8 mg of fumarate.

Acceptance criteria: 83.7–87.3 mg

IMPURITIES

• **Residue on Ignition** ⟨281⟩**:** NMT 0.1%

• **Organic Impurities**

Solution A, Buffer, Mobile phase, System suitability solution, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Sample: *Sample solution*

Calculate the area percentage of each impurity, relative to tiamulin fumarate, in the portion of Tiamulin Fumarate taken:

$$\text{Result} = (r_U/r_T) \times 100$$

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

r_T = peak response of tiamulin fumarate from the *Sample solution*

Acceptance criteria: See *Table 1*. Disregard the peak due to fumarate at a relative retention time of 0.15.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Pleuromutilin	0.25	1.0
Mutilin	0.3	1.0
14-Acetyl mutilin	0.5	1.0
11-Monoacetyl mutilin	0.6	1.0
Tiamulin related compound A	0.8	1.0
Tiamulin	1.0	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
11,14-Diacetyl mutilin	1.1	1.0
8-Dimethylderivative	1.3	1.0
Bisdimethylthioderivative	1.4	1.0
11-Ketoderivative	2.3	1.0
Any individual unspecified impurity	—	0.5
Total impurities	—	3.0

SPECIFIC TESTS

- **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

  Sample solution: 5.0 mg/mL in dioxane

  Acceptance criteria: +24° to +28°, on the dried basis, measured at 20°

- **pH** ⟨791⟩

  Sample solution: 10 mg/mL

  Acceptance criteria: 3.1–4.1

- **Loss on Drying** ⟨731⟩

  Analysis: Dry under vacuum at 105° for 3 h.

  Acceptance criteria: NMT 0.5%

- **Clarity and Color of Solution**

  Sample: 5 g

  Analysis: Transfer the *Sample* to a 100-mL volumetric flask. Dissolve in and dilute with water to volume.

  Acceptance criteria: The solution is clear and colorless, and its absorbances determined in a 1-cm cell at 400 and 650 nm are NMT 0.150 and 0.030 absorbance units, respectively.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at room temperature.
- **Labeling:** Label it to indicate that it is for veterinary use only.
- **USP Reference Standards** ⟨11⟩

  USP Tiamulin Fumarate RS

  USP Tiamulin Related Compound A RS

Tosyl pleuromutilin.

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

Topic/Question	Contact	Expert Committee
TIAMULIN FUMARATE	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

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