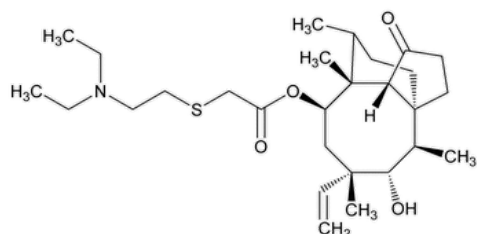


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Tiamulin



$C_{28}H_{47}NO_4S$ 493.74

Acetic acid, [[2-(diethylamino)ethyl]thio]-, 6-ethenyldecahydro-5-hydroxy-4,6,9,10-tetramethyl-1-oxo-3a,9-propano-3aH-cyclopentacycloocten-8-yl ester [3aS-(3a α ,4 β ,5 α ,6 α ,8 β ,9 α ,9a β ,10S*)]-; [[2-(Diethylamino)ethyl]thio]acetic acid 8-ester with (3aS,4R,5S,6S,8R,9R,9aR,10R)-octahydro-5,8-dihydroxy-4,6,9,10)-tetramethyl-6-vinyl-3a,9-propano-3aH-cyclopentacycloocten-1(4H)-one CAS RN[®]: 55297-95-5; UNII: E38WZ4U54R.

DEFINITION

Tiamulin contains NLT 96.5% and NMT 102.0% of tiamulin ($C_{28}H_{47}NO_4S$), calculated on the dried basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197A or 197K.
- **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

Buffer: Dissolve 10.0 g of [ammonium carbonate](#) in [water](#), add 22 mL of [perchloric acid TS](#), and dilute with [water](#) to 1000 mL. Adjust with [ammonium hydroxide](#) to a pH of 10.0.

Mobile phase: [Methanol](#), [acetonitrile](#), and *Buffer* (490:210:300)

Diluent: [Acetonitrile](#) and *Buffer* (1:1)

Standard solution: 5.0 mg/mL of [USP Tiamulin Fumarate RS](#) in *Diluent*

Sample solution: 4.0 mg/mL of Tiamulin in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 212 nm

Column: 4.6-mm $\times$ 15-cm; 5- μ m packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 20 μ L

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2 between tiamulin and its subsequent peak

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

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

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

M_{r1} = molecular weight of tiamulin, 493.74

M_{r2} = molecular weight of tiamulin fumarate, 609.82

Acceptance criteria: 96.5%–102.0% on the dried basis

IMPURITIES

• LIMIT OF ALCOHOL AND TOLUENE

Proceed as directed in [Residual Solvents \(467\)](#).

Acceptance criteria

Alcohol: NMT 1.0%

Toluene: NMT 0.08%

Sum of alcohol and toluene: NMT 1.0%

Change to read:

• ORGANIC IMPURITIES

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

Toluene solution: Transfer 0.1 mL of [toluene](#) to a 100-mL volumetric flask, and dilute with [acetonitrile](#) to volume. Transfer 0.1 mL of this solution to another 100-mL volumetric flask, and dilute with *Diluent* to volume.

Diluted sample solution: 0.04 mg/mL of Tiamulin from the *Sample solution* in *Diluent*

Analysis

Samples: *Standard solution, Sample solution, Toluene solution, and Diluted sample solution*

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

$$\text{Result} = (r_U/r_T) \times \Delta_D \times 100 \quad (\text{ERR 1-Dec-2020})$$

r_U = peak area of each individual impurity from the *Sample solution*

r_T = peak area of tiamulin from the *Diluted sample solution*

Δ_D = dilution factor for the *Sample solution*, 0.01 (ERR 1-Dec-2020)

Acceptance criteria: See [Table 1](#). Disregard the toluene peak and any peak from the *Sample solution* less than 0.1 times the area of the principal peak from the *Diluted sample solution*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Mutilin	0.22	1.0
2-(Benzylsulfanyl)-N,N-diethylethanamine	0.50	1.0
2,2'-(Disulfane-1,2-diyl)bis(N,N-diethylethanamine)	0.66	1.0
Tiamulin	1.0	1.0
Hydroxy-11-oxotiamulin	1.1	1.0