Epothilone D

Cat. No.: HY-15278

CAS No.: 189453-10-9

Molecular Formula: $C_{27}H_{41}NO_5S$

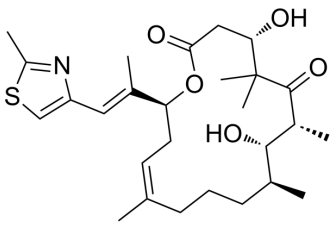
Molecular Weight: 491.68

Target: Microtubule/Tubulin; Fungal; Bacterial; Antibiotic

Pathway: Cell Cycle/DNA Damage; Cytoskeleton; Anti-infection

Storage:

Powder	-20°C	3 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (203.38 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0338 mL	10.1692 mL	20.3384 mL
5 mM	0.4068 mL	2.0338 mL	4.0677 mL
10 mM	0.2034 mL	1.0169 mL	2.0338 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.08 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.08 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Epothilone D (KOS 862) is a potent microtubule stabilizer.

IC_{50} & Target

Microtubule/Tubulin[1]

In Vitro

Epothilone D (KOS-862) is a more potent microtubule stabilizer in vitro than epothilone A or B. In vitro, Epothilone D has shown potent cytotoxicity in a panel of human tumor cell lines, with similar potency to paclitaxel. Epothilone D also shows a definite advantage over paclitaxel in drug-resistant cell lines, and retained its cytotoxicity against a multidrug resistant cell line over-expressing P-glycoprotein[1]. Epothilone D (EpoD) is a microtubules (MTs)-stabilizing agent[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo	To evaluate whether Epothilone D (EpoD) improves MT and axonal function in PS19 mice, groups of 3-month old male PS19 mice received weekly i.p. injections of vehicle or Epothilone D (EpoD) (1 mg/kg or 3 mg/kg) for a total of 3 months. In addition, 3-month old non-Tg littermates received 3 mg/kg Epothilone D (EpoD) or vehicle. The 3 mg/kg Epothilone D (EpoD) dose corresponds to ~10-fold less than that used in a Phase II clinical study, which should minimize side-effects such as neutropenia that are observed with MT-stabilizing drugs in human subjects. PS19 and WT mice that receive Epothilone D (EpoD) show no signs of drug intolerance. Indeed, all drug-treated mice exhibited weight gain that is indistinguishable from vehicle-treated animals. Likewise, relative organ weights are similar in vehicle- and Epothilone D (EpoD)-treated mice. The motor performance of Epothilone D (EpoD)-treated mice, assessed using a standard rotarod test, is not significantly different from vehicle-treated cohorts. Finally, although there is minor group-to-group variability, there are no significant differences in white blood cell counts or neutrophil content between any of the treatment cohorts. Thus, the low doses of Epothilone D (EpoD) utilized in these studies appeared to be well tolerated[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Mice[2] Groups of mice (n=3) receive intraperitoneal (i.p.) injections of 3.7 mg/kg of Epothilone D (epoD) dissolved in 100% DMSO, followed by euthanization using approved at times ranging from 0.25 h to 24 h. In another study, groups of mice (n=3) receive injections of 3 mg/kg of epoD in 100% DMSO followed by euthanization 4, 6 and 10 days later. The Epothilone D (epoD) levels in brain and blood samples are determined using LC-MS/MS protocols. Groups (n=10-13) of 3-month old PS19 tau Tg mice or 3-month old non-Tg littermates are administered weekly i.p. injections of 1 mg/kg epoD, 3 mg/kg of Epothilone D (epoD) or vehicle (DMSO), for a total of 3 months. Animals are monitored for signs of abnormal behavior or distress, and are weighed weekly. After final dosing, the mice undergo motor function and cognitive testing. After euthanization, brains and optic nerve (ON) are recovered for immunohistochemical analyses. A subset of mice from each group also undergo necropsy evaluation with organ weights recorded. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Front Mol Neurosci. 2023 Oct 12:16:1198299.
- Sci Rep. 2020 Sep 8;10(1):14776.
- Chemical Biology. Harvard University. 2019 May.

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REFERENCES

[1]. Konner J, et al. Phase I clinical, pharmacokinetic, and pharmacodynamic study of KOS-862 (Epothilone D) in patients with advanced solid tumors and lymphoma. Invest New Drugs. 2012 Dec;30(6):2294-302.

[2]. Brunden KR, et al. Epothilone D improves microtubule density, axonal integrity, and cognition in a transgenic mouse model of tauopathy. J Neurosci. 2010 Oct 13;30(41):13861-6.

Caution: Product has not been fully validated for medical applications. For research use only.

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