Epothilone B

Cat. No.: HY-17029

CAS No.: 152044-54-7

Molecular Formula: $C_{27}H_{41}NO_6S$

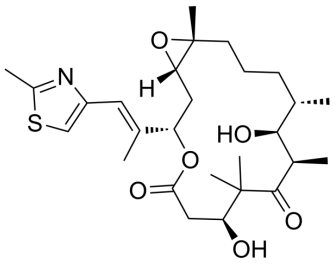
Molecular Weight: 507.68

Target: Microtubule/Tubulin; Apoptosis; Fungal; Antibiotic; Bacterial

Pathway: Cell Cycle/DNA Damage; Cytoskeleton; Apoptosis; 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 (196.97 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9697 mL	9.8487 mL	19.6974 mL
	5 mM	0.3939 mL	1.9697 mL	3.9395 mL
	10 mM	0.1970 mL	0.9849 mL	1.9697 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: ≥ 2.08 mg/mL (4.10 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.10 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.08 mg/mL (4.10 mM); Clear solution; Need warming

BIOLOGICAL ACTIVITY

Description

Epothilone B is a microtubule stabilizer with a K_i of 0.71μM. It acts by binding to the αβ-tubulin heterodimer subunit which causes decreasing of αβ-tubulin dissociation.

IC_{50} & Target

EC0.01: 1.8 μM (Microtubule/Tubulin)[1]

In Vitro

Epothilone B inhibits HCT116 cells with IC_{50} of 0.8 nM in HCT-116 cell line cytotoxicity assay[1]. Epothilone B (Patupilone) is a microtubule (MT) targeting agent. As shown by MTT cell proliferation assay, after 72 h of treatment Epothilone B efficiently inhibits cell growth with an IC_{50} of 6 nM, while concentrations ≤1 nM are not cytotoxic. Epothilone B significantly inhibits

transwell cell migration at the non-cytotoxic concentration of 1 nM, and the effect is more evident at 10 nM[2]. Epothilone B (Patupilone) is a novel, non-taxane-related and nonneurotoxic microtubule-stabilizing agent in human medulloblastoma cell lines. Epothilone B reduces the proliferative activity in the D341 cell line, with an IC_{50} of 0.53 nM; in the D425Med cell line, with an IC_{50} of 0.37 nM; and in the DAOY cell line, with an IC_{50} of 0.19 nM. In the D341Med cell line, the effect of Epothilone B on clonogenic survival is at dose range of Epothilone B similar to the level of proliferative activity and viability (IC_{50}, 0.50-0.75 nM). However, the clonogenicity of D425Med and DAOY cells is already strongly reduced at a 10-fold lower concentration of Epothilone B (IC_{50}, 30 pM). These results overall demonstrate that Epothilone B is highly potent against different medulloblastoma cell lines[3].

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

In Vivo

Treatment with Epothilone B (Patupilone) or ionizing radiation alone results in a partial tumor growth suppression over 10 days, whereas combined treatment exerts a strong supra-additive tumor growth control, with complete tumor regression in the follow-up period ($P<0.005$, for ionizing radiation or Epothilone B alone vs combined treatment)[3].

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PROTOCOL

Kinase Assay [3]

Asp-Glu-Val-Asp (DEVD)ase activity is determined in cytosolic cell extracts. Cells are treated with increasing concentrations of Epothilone B (Patupilone) for 6, 12, 24, and 48 h. Cells are harvested thereafter by trypsin/EDTA, centrifuged, and washed with precooled PBS. The cell pellet is suspended in 5 volumes of precooled buffer A (20 mM HEPES-KOH [pH 7.5], 10 mM KCl, 1.5 mM $MgCl_2$, 1 mM sodium EDTA, 1 mM sodium EGTA, 1 mM dithiothreitol [DDT], 250 mM sucrose, and 0.1 mM phenylmethylsulfonyl fluoride [PMSF] supplemented with protease inhibitors [5 mg/mL pepstatin A, 10 mg/mL leupeptin, 2 mg/mL aprotinin, 2 mg/mL DTT, and 1 mM of PMSF]). After incubation on ice for 15 min, the cells are disrupted by freezing and thawing. Cell lysates are centrifuged at 1000g for 10 min at 4°C, and the supernatant is further centrifuged at 100 000g for 30 min. The resulting supernatant (S-100 fraction) is stored at −80°C. To determine caspase 3-like activity, 75 µg of protein from the S-100 fraction is incubated at 37°C with the colorimetric caspase 3 substrate N-acetyl-Asp-Glu-Val-Asp p-nitroanilide (100 mM; Ac-DEVD-pNA) and 1 mM dATP in a final volume of 120 µL. Cleavage of the caspase substrate is monitored at 405 nm using a GenTec spectrophotometer[3].

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Cell Assay [2]

Human glioblastoma cells (U87MG, ATCC) are routinely maintained at 37°C and 5% CO_2 in EMEM medium, with NEAA, containing 10% fetal bovine serum, 2 mM of glutamine, 1% penicillin and streptomycin. U87MG cells are used for no more than 15 passages. Cells are seeded in 96-well plates (5000 cells/well). After 24 h cells are treated with Epothilone B. Growth inhibition of U87MG cells is measured after 72 h of drug treatment by using the MTT cell proliferation assay[2].

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Animal Administration [3]

Mice[3]

D425Med cells (6×10^6) are injected subcutaneously on the backs of 4-6-week-old athymic nude mice. Tumor volumes are determined from caliper measurements of tumor length (L) and width (l) according to the formula $(L\times l^2)/2$. Tumors are allowed to expand to a volume of 200 mm^3 (±10%) before treatment start. With the use of a customized shielding device, mice are given strictly loco regional radiotherapy of 3×3 Gy on 3 consecutive days using a Gulmay 200 kV X-ray unit at 100 cGy/min at room temperature. Epothilone B (2 mg/kg; dissolved in 30% PEG-300/70% saline) is applied intravenously 24 h before the first treatment with ionizing radiation (at day 0 of the treatment; n=5 per group). Tumor growth is monitored daily.

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CUSTOMER VALIDATION

- Am J Pathol. 2021 Sep 23;S0002-9440(21)00393-X.

- Eur J Pharm Sci. 2022 Dec 7;106350.
- Biochem Biophys Res Commun. 2021 Jan 1;534:330-336.
- bioRxiv. 2021 Feb 5.
- Oncotarget. 2017 Dec 2;8(68):112313-112329.

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REFERENCES

[1]. Regueiro-Ren A, et al. Synthesis and biological activity of novel epothilone aziridines. Org Lett. 2001 Aug 23;3(17):2693-6.

[2]. Pagano A, et al. Epothilone B inhibits migration of glioblastoma cells by inducing microtubule catastrophes and affecting EB1 accumulation at microtubule plus ends. Biochem Pharmacol. 2012 Aug 15;84(4):432-43.

[3]. Oehler C, et al. The microtubule stabilizer patupilone (epothilone B) is a potent radiosensitizer in medulloblastoma cells. Neuro Oncol. 2011 Sep;13(9):1000-10.

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

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