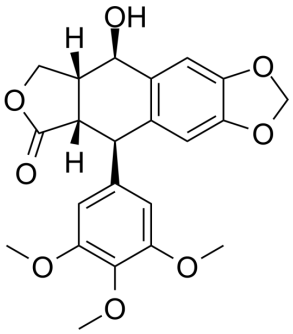
Picropodophyllin



Cat. No.:	HY-15494
CAS No.:	477-47-4
Molecular Formula:	$C_{22}H_{22}O_8$
Molecular Weight:	414.41
Target:	IGF-1R; Apoptosis
Pathway:	Protein Tyrosine Kinase/RTK; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month

SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (120.65 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4131 mL	12.0653 mL	24.1307 mL
	5 mM	0.4826 mL	2.4131 mL	4.8261 mL
	10 mM	0.2413 mL	1.2065 mL	2.4131 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.03 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Picropodophyllin (AXL1717) is a selective insulin-like growth factor-1 receptor (IGF-1R) inhibitor with an IC_{50} of 1 nM.

IC_{50} & Target

IC50: 1 nM (IGF-1R)

In Vitro

Picropodophyllin (AXL1717) (0.5, 2.5, 10 μM) potently inhibits IGF-1-stimulated IGF-1R, Akt (Ser 473) and Erk1/2 phosphorylation in intact cells. Picropodophyllin (AXL1717) also inhibits cell growth, and induces apoptosis in cultured IGF-1R-positive tumor cells[1]. Picropodophyllin (AXL1717) synergistically sensitizes HMCL, primary human MM and murine 5T33MM cells to ABT-737 and ABT-199 via further decreasing cell viability and enhancing apoptosis[3]. Picropodophyllin and sorafenib synergistically suppress the proliferation and motility of hepatocellular carcinoma cells[4].

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

In Vivo

Picropodophyllin (AXL1717) (20 mg/kg/12 h, i.p.) causes complete tumor regression in SCID mice xenografted with human

ES-1, BE, and PC3[1]. Picropodophyllin (AXL1717) shows a potent antitumor activity, increases survival in the 5T33MM mouse model[2].

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PROTOCOL

Animal Administration [1]

Four to 5-week-old pathogen-free SCID mice are used and housed within plastic isolators in a sterile facility. ES-1, BE, and PC3 cells (all proved to express IGF-1R), or R-v-src (IGF-1R negative) and P12 (overexpressing IGF-1 and IGF-1R), are injected s.c. at 10^7 cells/mice in a 0.2 mL volume of sterile saline solution. Immunocompetent Balb-c mice are injected with 107JC murine breast cancer cells per mouse in 0.15 mL volume of sterile saline solution. Experimental treatments with Picropodophyllin (AXL1717) (20 mg/kg/12 h) are performed by daily i.p. injections of the compound in 10 μL volume of DMSO: vegetable oil, 10:1 (v/v). Control mice are treated with the vehicle only. Three animals are treated in each group. Tumor growth is measured every second day using vernier calipers, and the tumor volumes are calculated. The mice are carefully observed for the presence of side effects and are sacrificed at the end of the experiments for histological analysis of the lesions. A separate experiment on Picropodophyllin (AXL1717)-treated (systemically and locally) tumor-free mice, including histological analyses of various organs, confirms previous observations that Picropodophyllin (AXL1717) appears to be nontoxic.

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

CUSTOMER VALIDATION

- Science. 2017 Dec 1;358(6367):eaan4368.
- Nat Nanotechnol. 2021 Jul;16(7):830-839.
- EMBO J. 2019 Aug 1;38(15):e101964.
- Environ Sci Technol. 2020 Sep 1;54(17):10783-10796.
- Cell Death Dis. 2022 Aug 5;13(8):682.

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REFERENCES

[1]. Girnita A, et al. Cyclolignans as inhibitors of the insulin-like growth factor-1 receptor and malignant cell growth. Cancer Res. 2004 Jan 1;64(1):236-42.

[2]. Menu E, et al. Inhibiting the IGF-1 receptor tyrosine kinase with the cyclolignan PPP: an in vitro and in vivo study in the 5T33MM mouse model. Blood. 2006 Jan 15;107(2):655-60. Epub 2005 Jul 26.

[3]. Bieghs L, et al. The IGF-1 receptor inhibitor picropodophyllin potentiates the anti-myeloma activity of a BH3-mimetic. Oncotarget. 2014 Nov 30;5(22):11193-208.

[4]. Tomizawa M, et al. Picropodophyllin and sorafenib synergistically suppress the proliferation and motility of hepatocellular carcinoma cells. Oncol Lett. 2014 Nov;8(5):2023-2026. Epub 2014 Aug 27.

[5]. Stromberg T, et al. IGF-1 receptor tyrosine kinase inhibition by the cyclolignan PPP induces G2/M-phase accumulation and apoptosis in multiple myeloma cells. Blood. 2006 Jan 15;107(2):669-78. Epub 2005 Sep 15.

[6]. Kong YL, et al. Insulin deficiency induces rat renal mesangial cell dysfunction via activation of IGF-1/IGF-1R pathway. Acta Pharmacol Sin. 2016 Feb;37(2):217-27.

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

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