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Zuschläge

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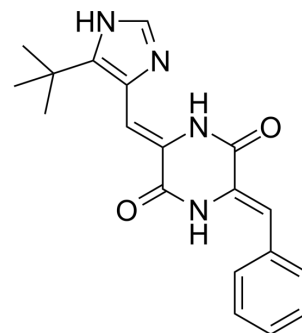
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Plinabulin

Cat. No.:	HY-14444
CAS No.:	714272-27-2
Molecular Formula:	C ₁₉ H ₂₀ N ₄ O ₂
Molecular Weight:	336.39
Target:	Microtubule/Tubulin
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro	DMSO : 50 mg/mL (148.64 mM; Need ultrasonic)					
	Preparing Stock Solutions	Solvent Concentration	Mass	1 mg	5 mg	10 mg
		1 mM		2.9727 mL	14.8637 mL	29.7274 mL
		5 mM		0.5945 mL	2.9727 mL	5.9455 mL
		10 mM		0.2973 mL	1.4864 mL	2.9727 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 (7.43 mM); Clear solution					
	2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (7.43 mM); Suspended solution; Need ultrasonic					
	3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (7.43 mM); Clear solution					

BIOLOGICAL ACTIVITY

Description	Plinabulin (NPI-2358) is a vascular disrupting agent (VDA) against tubulin-depolymerizing with an IC ₅₀ of 9.8 nM against HT-29 cells ^[1] . Plinabulin binds the colchicine binding site of β-tubulin preventing polymerization and has potent inhibitory to tumor cells ^[2] .
IC ₅₀ & Target	β-tubulin ^[2]
In Vitro	Plinabulin (NPI-2358) (2-200 nM; 30 minutes; HUVECs cells) is a potent anti-tumor agent which is active in multidrug-

resistant (MDR) tumor cell lines, and is able to rapidly induce tubulin depolymerization and monolayer permeability in HUVECs, with IC₅₀ values of 18 nM for DU 145 cells; 13 nM for PC-3 cells; 14 nM for MDA-MB-231 cells; 18 nM for NCI-H292 cells; and 11 nM for Jurkat leukemia cells^[1].

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

Cell Viability Assay^[1]

Cell Line:	HUVECs cells
Concentration:	2 nM, 10 nM, 20 nM and 200 nM
Incubation Time:	30 minutes
Result:	Low concentrations (2 nM, 10 nM) rapidly induced tubulin depolymerization in HUVECs.

In Vivo

Plinabulin (0 mg/kg-15 mg/kg; intraperitoneal injection; female CDF1 and C3H/He mice) induces a time- and dose-dependent decrease in tumor perfusion. The KHT sarcoma is more sensitive than the C3H tumor to the anti-tumor effects of Plinabulin, while radiation response is enhanced in both models^[3].

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

Animal Model:	Female CDF1 mice (10-14-week-old) with C3H mammary carcinoma; Female C3H/HeJ mice with KHT sarcoma cells (8-weeks-old) ^[3]
Dosage:	0 mg/kg, 1.5 mg/kg, 2.5 mg/kg, 5 mg/kg, 7.5 mg/kg, 10 mg/kg, 12.5 mg/kg, 15 mg/kg; 0.02 mL/g mouse body weight in CDF1 mice and 0.01 mL/g body weight for C3H/HeJ mice
Administration:	Intraperitoneal injection; 0 hour, 1 hour, 3 hours, 6 hours, 24 hours
Result:	Induced a time- and dose-dependent decrease in tumour perfusion. The KHT sarcoma was more sensitive than the C3H tumour to the anti-tumor, while radiation response was enhanced in both models.

REFERENCES

- [1]. Nicholson B et al. NPI-2358 is a tubulin-depolymerizing agent: in-vitro evidence for activity as a tumor vascular-disrupting agent. *Anticancer Drugs*. 2006 Jan;17(1):25-31.
- [2]. Monica M. Mita et al. Phase 1 First-in-Human Trial of the Vascular Disrupting Agent Plinabulin (NPI-2358) in Patients with Solid Tumors or Lymphomas *Clin Cancer Res*. 2010 Dec 1;16(23):5892-9.
- [3]. Bertelsen LB, et al. Vascular effects of plinabulin (NPI-2358) and the influence on tumour response when given alone or combined with radiation. *Int J Radiat Biol*. 2011 Nov;87(11):1126-34.

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

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