Combretastatin A-1

Cat. No.: HY-121993

CAS No.: 109971-63-3

Molecular Formula: $C_{18}H_{20}O_6$

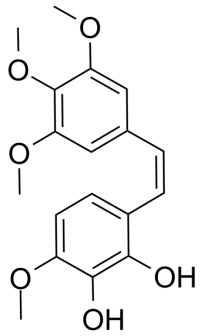
Molecular Weight: 332.35

Target: Microtubule/Tubulin

Pathway: Cell Cycle/DNA Damage; Cytoskeleton

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 : ≥ 100 mg/mL (300.89 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.0089 mL	15.0444 mL	30.0888 mL
5 mM	0.6018 mL	3.0089 mL	6.0178 mL
10 mM	0.3009 mL	1.5044 mL	3.0089 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 (6.26 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.26 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (6.26 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Combretastatin A-1 is a microtubule polymerization inhibitor that binds to the colchicine-binding site of tubulin. Combretastatin A-1 inhibits the Wnt/β-catenin pathway through tubulin depolymerization mediated AKT deactivation. Combretastatin A-1 exhibits anti-tumor and anti-vascular effects[1][2][3].

IC_{50} & Target

Microtubule/Tubulin[1]

In Vitro

Combretastatin A-1 (72 h) inhibits the growth of various tumor cell lines in vitro, including HepG2, SMMC-7721, Hepa 1-6, LM-3, Bel-7402, Huh7, BGC-803, MDA-MB-231, MCF-7, A375, NCI-1975, CT-26, HT-29, A549 cells (IC_{50}=9.2, 12.8, 32.9, 33.8, 38.4, 728.2, 12.2, 17.6, 46.0, 61.0, 256.3, 1075.0, 2082.0, 2247.0 nM, respectively)[2].

Combretastatin A-1 (1-10 nM; 24 h) induces apoptosis by microtubule depolymerization-induced AKT inactivation and the removal of GSK-3β inhibition in HepG2 cells[2].

Combretastatin A-1 (1-50 nM; 6 h) decreases the mitochondrial membrane potential (MMP) of HepG2 cells. Combretastatin A-1 shows dose-dependently ROS accumulation in HepG2 cells[2].

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

Western Blot Analysis[2]

Cell Line:	HepG2 cells
Concentration:	1, 5, 10 nM
Incubation Time:	24 hours
Result:	Significantly decreased Mcl-1 expression, but the Bcl-2 level was unchanged. Reduced p-GSK 3β (Ser9) without altering total GSK-3β protein levels, indicating an activation of GSK-3β. Reduced AKT phosphorylation on Ser473 without an obvious change in the total AKT protein levels.

In Vivo

Combretastatin A-1 (1-4 mg/kg; i.v. every other day for 4 weeks) significantly reduces the tumor volume in HepG2 subcutaneous xenograft model[2].

Combretastatin A-1 (2 mg/kg; every other day for 21 days) shows enhanced apoptosis in orthotopic hepatocellular carcinoma mouse model[2].

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

Animal Model:	Male athymic BALB/c nu/nu mice (16-18 g; 4-6 weeks old) were inoculated with HepG2 cells[2]
Dosage:	1, 2, 4 mg/kg
Administration:	I.v. every other day for 4 weeks
Result:	Resulted in a significant tumor volume reduction at the dose of 2 mg/kg or 4 mg/kg.

REFERENCES

[1]. Pettit GR, et, al. Isolation, structure, and synthesis of combretastatins A-1 and B-1, potent new inhibitors of microtubule assembly, derived from Combretum caffrum. J Nat Prod. Jan-Feb 1987;50(1):119-31.

[2]. Mao J, et, al. Combretastatin A-1 phosphate, a microtubule inhibitor, acts on both hepatocellular carcinoma cells and tumor-associated macrophages by inhibiting the Wnt/β-catenin pathway. Cancer Lett. 2016 Sep 28;380(1):134-43.

[3]. Holwell SE, et, al. Anti-tumor and anti-vascular effects of the novel tubulin-binding agent combretastatin A-1 phosphate. Anticancer Res. Nov-Dec 2002;22(6C):3933-40.

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