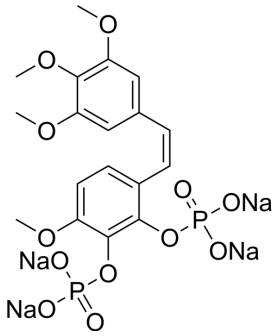
Combretastatin A-1 phosphate tetrasodium

Cat. No.:	HY-16146
CAS No.:	288847-34-7
Molecular Formula:	$C_{18}H_{18}Na_4O_{12}P_2$
Molecular Weight:	580.23
Target:	Microtubule/Tubulin
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Combretastatin A-1 phosphate (OXi-4503) tetrasodium, a proagent of Combretastatin A-1, is a microtubule polymerization inhibitor that binds to the colchicine-binding site of tubulin. Combretastatin A-1 phosphate tetrasodium inhibits the Wnt/β-catenin pathway through tubulin depolymerization mediated AKT deactivation. Combretastatin A-1 phosphate tetrasodium exhibits anti-tumor and anti-vascular effects[1][2][3].
IC_{50} & Target	Microtubule/Tubulin[1]
In Vitro	Combretastatin A-1 phosphate (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 phosphate (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 phosphate (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 phosphate (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 phosphate (2 mg/kg; every other day for 21 days) shows enhanced apoptosis in orthotopic hepatocellular carcinoma mouse model[2].

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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]. Stratford MRL, et, al. Quantitative determination of the anticancer prodrug combretastatin A1 phosphate (OXi4503, CA1P), the active CA1 and its glucuronide metabolites in human urine and of CA1 in plasma by HPLC with mass spectrometric detection. J Chromatogr B Analyt Technol Biomed Life Sci. 2012 Jun 1;898:1-6.

[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.

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

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