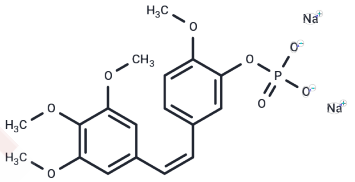
Data Sheet (Cat.No.T6272)

TargetMol

Fosbretabulin Disodium

Chemical Properties



CAS No. : 168555-66-6

Formula: C18H19O8P·2Na

Molecular Weight: 440.29

Appearance: no data available

Storage: store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Fosbretabulin Disodium (CA 4P), a water-soluble prodrug of Combretastatin A4 (CA4), is a microtubule-targeting agent that binds β-tubulin (Kd: 0.4 μM). Fosbretabulin Disodium(Combretastatin A4 disodium phosphate) inhibits the polymerization of tubulin (IC50: 2.4 μM), and also disrupts tumor vasculature.
Targets(IC50)	Apoptosis,Microtubule Associated
In vitro	Fosbretabulin disodium (Combretastatin A-4 phosphate disodium, CA4P disodium) is the water-soluble prodrug of combretastatin A4 (CA4), which is originally isolated from African tree Combretum caffrum. CA4 is a tubulin-binding agent that binds at or near the colchicine binding site of β-tubulin (Kd = 0.40 μM), inhibits tubulin assembly with IC50 of 2.4 μM. [1] CA4 is cytotoxic towards proliferating but not quiescent endothelial cells, has potent and selective toxicity towards tumor vasculature. [2] CA4P (1 mM, 30 minutes) disrupts the endothelial microtubule cytoskeleton and mediates changes in endothelial cell morphology. CA4P stimulates actin stress fiber formation and membrane blebbing and increases monolayer permeability via Rho/Rho-kinase. [3] CA4P increases endothelial cell permeability, while inhibiting endothelial cell migration and capillary tube formation predominantly through disruption of VE-cadherin/β-catenin/Akt signaling pathway, thereby leading to rapid vascular collapse and tumor necrosis. [4]
In vivo	CA4P causes rapid, extensive and irreversible vascular shutdown in experimental tumor models following the administration of a single dose at 10% of the maximum tolerated dose (MTD). CA4P causes a 93% reduction in vascular volume 6 h following drug administration. [2] CA4P(100 mg/kg, 6 h following administration) reduces tumor blood by approximately 100-fold, compared with approximately 7-fold in the spleen. [5]
Kinase Assay	Tubulin assembly-disassembly: The assembly of microtubules from isolated tubulin is carried out spectrophotometrically at 350 nm and utilises the increase in turbidity which is associated with microtubule formation. Assembly is initiated by temperature increase from 10 to 35 °C. The effect of drugs on the increase in light absorption is carried. Drugs are dissolved in DMSO (<4%), which does not affect control assembly
Cell Research	For the proliferation assay, the minimal concentration of FBS (1%) diluted in X-VIVO medium is used to allow sufficient viability of endothelial cells. After detachment, the cells are seeded at a concentration of 2×104 HUVECs in each well of 24-well plates, allowed to adhere overnight, and then incubated with or without cytokines (5 ng/ml FGF-2 or 5 ng/ml VEGF-A). CA4P is added at 0 - 50 nM. After incubation for 12, 24, 36,

	and 48 hours, cells are detached by trypsin/EDTA and manually counted using trypan blue exclusion. (Only for Reference)

Solubility Information

Solubility	H2O: 10 mM,Sonication is recommended. DMSO: Insoluble, (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2712 mL	11.3562 mL	22.7123 mL
5 mM	0.4542 mL	2.2712 mL	4.5425 mL
10 mM	0.2271 mL	1.1356 mL	2.2712 mL
50 mM	0.0454 mL	0.2271 mL	0.4542 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Woods JA, et al. Br J Cancer 1995, 71(4), 705-711.
Han T, Duan Q, Yang R, et al. Monitoring the therapeutic efficacy of CA4P in the rabbit VX2 liver tumor using dynamic contrast-enhanced MRI. Diagnostic and Interventional Radiology. 2021, 27(5): 587.
Meng F, Zou B, Yang R, et al. The diagnostic efficiency of the perfusion-related parameters in assessing the vascular disrupting agent (CA4P) response in a rabbit VX2 liver tumor model. Acta Radiologica. 2021: 02841851211032450.
Dark GG, et al. Cancer Res 1997, 57(10), 1829-1834.
Kathou C, et al. Blood, 2002, 99(6), 2060-2069.
Vincent L, et al. J Clin Invest, 2005, 115(11), 21992-32006.
Tozer GM, et al. Cancer Res, 1999, 59(7), 1626-1634.