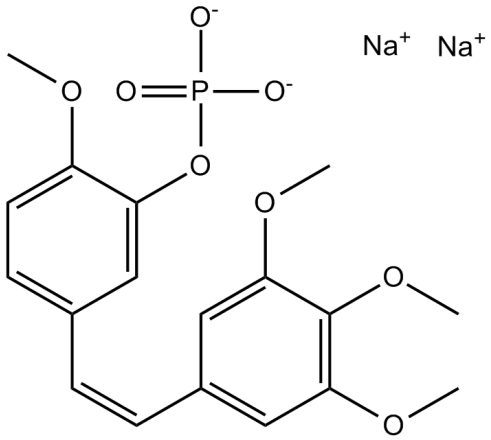
Product Data Sheet

Product Name: Fosbretabulin (Combretastatin A4 Phosphate (CA4P)) Disodium
Cat. No.: GC12308

Chemical Properties

Cas. No.	168555-66-6		
Chemical Name	disodium;[2-methoxy-5-[(Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]phenyl] phosphate		
SMILES	COC1=C(C=C(C=C1)C=CC2=CC(=C(C(=C2)OC)OC)OC)OP(=O)([O-])[O-].[Na+].[Na+]		
Formula	C18H19Na2O8P	M.Wt	440.29
Solubility	≥ 11.7mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Cell lines MCF-7 cells

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Preparation Method	MCF-7 cells were cultured in RPMI 1640 medium supplemented with 10% fetal bovine serum, 100units /ml penicillin and 100μg/ml streptomycin at 37°C, 5% CO_2, and high humidity. Cells were seeded in standard 96-well microplates at a density of approximately 5×10^5 cells/well and cultured for 24h to allow adherence. Cells were incubated with different concentrations of Fosbretabulin Disodium (0.0001, 0.001, 0.01, 0.1, 1.0, and 10μM) for 48 hours. Cells were fixed at the bottom of each well with ice-cold 50% trichloroacetic acid (TCA) and incubated for 2h at 4°C. After washing and drying, the cells were stained with 70μl of 0.4% (w/v) SRB for 10min (room temperature), washed five more times with 1% acetic acid, and air dried. The bound dye was dissolved with 100μl of 10mM Tris base solution, and the optical density values were determined at 515nm.
Reaction Conditions	0.0001, 0.001, 0.01, 0.1, 1.0, and 10μM; 48h
Applications	Fosbretabulin Disodium treatment inhibited the cell viability of MCF-7 cells in a dose-dependent manner.

Animal experiment [2]:

Animal models	Male Wistar albino rats

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Preparation Method	Male Wistar albino rats weighing 140 to 160g were maintained under standard conditions and had ad libitum access to fresh water and feed. A total of 126 rats were randomly divided into 7 groups (n=18). (I) normal control group: rats were given normal saline orally during the experiment. (II) Fosbretabulin Disodium group; Normal rats received Fosbretabulin Disodium (10mg/kg) intravenously. (III) LDR group: normal rats were exposed to a single low dose of γ-rays (0.20Gy; 0.685rad/s). (IV) NDEA/HCC group: rats were treated with NDEA (20mg/kg; 5 times a week for 8 weeks) followed by NDEA (10mg/kg, 5 times a week for 9 weeks) to induce hepatocellular carcinoma (HCC). (V) NDEA/HCC+LDR group: rats were treated with NDEA followed by low-dose γ-ray irradiation (0.20Gy; 0.685rad/s). (VI) NDEA/HCC+Fosbretabulin Disodium: rats were treated with NDEA followed by intravenous injection of Fosbretabulin Disodium (10mg/kg). All groups were sacrificed 24 hours after treatment, and rat livers were collected for analysis.
Dosage form	10mg/kg for once; i.v.
Applications	Fosbretabulin Disodium treatment combined with low-dose γ-ray irradiation repressed the expression of CD31 and gene expression of ROCK1 and VEGF in rats.

References:

[1] Liu Y, Wu Y, Gu Y, et al. Synthesis and structure-activity relationship study of water-soluble carbazole sulfonamide derivatives as new anticancer agents[J]. European journal of medicinal chemistry, 2020, 191: 112181.
[2] Alghzzawy Z M, Elmaghraby T K, El-Hamid Hagag S A, et al. Combretastatin A-4 disodium phosphate and low dose gamma irradiation suppress hepatocellular carcinoma by downregulating ROCK1 and VEGF gene expression[J]. Molecular biology reports, 2020, 47(3): 1883-1893.

Background

Fosbretabulin (Combretastatin A4 Phosphate (CA4P)) Disodium is a microtubule destabilizing drug, a water-soluble prodrug of combretasain A4(CA4) [1]. Fosbretabulin Disodium can be

dephosphorylated in the body to form the active metabolite CA4, which promotes microtubule polymerization and thereby induces G2/M phase cell cycle arrest[2]. Fosbretabulin Disodium has been widely used to induce tumor necrosis and is employed as an adjuvant to develop new combined therapies[3].

In vitro, Fosbretabulin Disodium treatment for 48 hours significantly inhibited the proliferation of HepG2, Bel-7402, and MCF-7 cells, with IC_{50} values of 0.002μM, 0.04μM, and 0.011μM, respectively[4]. Fosbretabulin Disodium treatment at 1μM for 30min disrupted the microtubule skeleton of human umbilical vein endothelial cells (HUVECs) and altered cell morphology[5].

In vivo, Fosbretabulin Disodium treatment, administered by tail vein bolus (60mg/10ml/kg; 24h interval; four doses), resulted in multifocal necrosis, inflammatory cell infiltration, and telangiectasia in the myocardium of rats [6]. A single intraperitoneal injection of Fosbretabulin Disodium at a dose of 100mg/kg for 30min resulted in a rapid decrease in tumor perfusion followed by a subsequent decrease in interstitial fluid pressure in the C3H breast cancer mouse model[7]. A single intravenous injection of Fosbretabulin Disodium (10mg/kg) combined with low-dose γ-ray irradiation (0.20Gy; 0.685rad/sec) treatment for 24h inhibited N-nitrosodiethylamine (NDEA)-induced hepatocellular carcinoma development in rats by down-regulating CD31 expression and gene expression of ROCK1 and VEGF[8].

References:
[1] Smolarczyk R, Czapla J, Jarosz-Biej M, et al. Vascular disrupting agents in cancer therapy[J]. European journal of pharmacology, 2021, 891: 173692.
[2] Lu Y, Chen J, Xiao M, et al. An overview of tubulin inhibitors that interact with the colchicine binding site[J]. Pharmaceutical research, 2012, 29(11): 2943-2971.
[3] Nagaiah G, Remick S C. Combretastatin A4 phosphate: a novel vascular disrupting agent[J]. Future Oncology, 2010, 6(8): 1219-1228.
[4] Liu Y, Wu Y, Gu Y, et al. Synthesis and structure-activity relationship study of water-soluble carbazole sulfonamide derivatives as new anticancer agents[J]. European journal of medicinal chemistry, 2020, 191: 112181.
[5] Kanthou C, Tozer G M. The tumor vascular targeting agent combretastatin A–4-phosphate induces reorganization of the actin cytoskeleton and early membrane blebbing in human endothelial cells[J]. Blood, The Journal of the American Society of Hematology, 2002, 99(6): 2060-2069.

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[6] Tochinai R, Nagata Y, Ando M, et al. Combretastatin A4 disodium phosphate-induced myocardial injury[J]. Journal of toxicologic pathology, 2016, 29(3): 163-171.
[7] Ley C D, Horsman M R, Kristjansen P E G. Early effects of combretastatin-A4 disodium phosphate on tumor perfusion and interstitial fluid pressure[J]. Neoplasia, 2007, 9(2): 108-112.
[8] Alghzzawy Z M, Elmaghraby T K, El-Hamid Hagag S A, et al. Combretastatin A-4 disodium phosphate and low dose gamma irradiation suppress hepatocellular carcinoma by downregulating ROCK1 and VEGF gene expression[J]. Molecular biology reports, 2020, 47(3): 1883-1893.

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