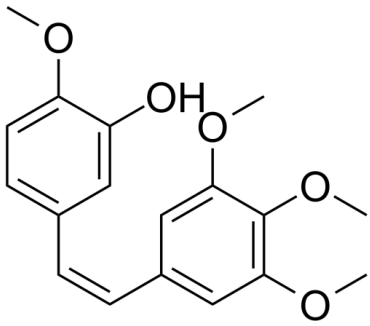
Data Sheet

Product Name:	Combretastatin A4
Cat. No.:	CS-6023
CAS No.:	117048-59-6
Molecular Formula:	C18H20O5
Molecular Weight:	316.35
Target:	Microtubule/Tubulin
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton
Solubility:	H2O : < 0.1 mg/mL (insoluble); DMSO : 100 mg/mL (316.11 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Combretastatin A4 is a **microtubule**-targeting agent that binds **β-tubulin** with K_d of 0.4 μM. IC50 & Target: Kd: 0.4 μM (β-tubulin) **In Vitro:** Combretastatin A4 phosphate (≥ 50 μM) significantly increases the percentage of annexin-V-binding cells and significantly decreases forward scatter. Combretastatin A4 phosphate does not appreciably increase hemolysis. Hundred μM Combretastatin A4 phosphate significantly increases Fluo3-fluorescence. The effect of Combretastatin A4 phosphate (100 μM) on annexin-V-binding is significantly blunted, but not abolished, by removal of extracellular Ca^{2+}. Combretastatin A4 phosphate (≥ 50 μM) significantly decreases GSH abundance and ATP levels but does not significantly increase ROS or ceramide[2]. Polymersomes co-encapsulating doxorubicin-combretastatin-A4 phosphate (1:10) shows strong synergistic cytotoxicity against human nasopharyngeal epidermal carcinoma (KB) cells[3]. Pretreatment with Combretastatin A4 phosphate does not influence the amount of VM in 3-D culture as well as the expression of these key molecules[4]. **In Vivo:** DBP and MBP at 30 minutes after administration are higher in rats treated with Combretastatin A4 disodium phosphate 120 mg/10 mL/kg. The toxicokinetic parameters of Combretastatin A4 phosphate and Combretastatin A4 in rats treated with Combretastatin A4 disodium phosphate 120 mg/10 mL/kg are indicated, and the values of Cmax, T1/2, and AUC0-inf for Combretastatin A4 are 156±13 μM, 5.87±1.69 h, and 89.4±10.1 h·μM, respectively[1]. In vivo, W256 tumors show marked intratumoral hypoxia after Combretastatin A4 phosphate treatment, accompanied by increased VM formation. Combretastatin A4 phosphate exhibits only a delay in tumor growth within 2 days but rapid tumor regrowth afterward. VM density is positively related to tumor volume and tumor weight at day 8. Combretastatin A4 phosphate causes hypoxia which induces VM formation in W256 tumors through HIF-1α/EphA2/PI3K/matrix metalloproteinase (MMP) signaling pathway, resulting in the consequent regrowth of the damaged tumor[4].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: [1]Rats are administered a single intravenous dose of Combretastatin A4 disodium phosphate at 120 mg/10 mL/kg by bolus infusion (n=3). Blood is taken via the jugular vein and collected in heparin-coated tubes at 10 minutes and 1, 3, 6, and 24 hours after administration. Plasma is separated by centrifugation immediately after sampling. After centrifugation, an aliquot of plasma is mixed with the equivalent volume of 1% formic acid and stored at −20°C. The thawed plasma samples are purified by solid-phase extraction, and the plasma concentrations of combretastatin A4 phosphate (free base of Combretastatin A4 disodium phosphate; Combretastatin A4 phosphate) and combretastatin A4 (the metabolite of Combretastatin A4 disodium phosphate; Combretastatin A4) are determined by liquid chromatography-tandem mass spectrometry (LC-MS/MS). Toxicokinetic parameters [maximum concentration (Cmax), terminal half-life (T1/2), and area under the concentration-time curve from time zero to infinity (AUC0-inf)] are obtained by non-compartmental analysis using Phoenix WinNonlin 6.3.

References:

[1]. Tochinai R, et al. Combretastatin A4 disodium phosphate-induced myocardial injury. J Toxicol Pathol. 2016 Jul;29(3):163-71.

[2]. Signoretto E, et al. Stimulation of Eryptosis by Combretastatin A4 Phosphate Disodium (CA4P). Cell Physiol Biochem. 2016;38(3):969-8

[3]. Zhu J, et al. Co-Encapsulation of Combretastatin-A4 Phosphate and Doxorubicin in Polymersomes for Synergistic Therapy of Nasopharyngeal Epidermal Carcinoma. J Biomed Nanotechnol. 2015 Jun;11(6):997-1006.

[4]. Yao N, et al. Combretastatin A4 phosphate treatment induces vasculogenic mimicry formation of W256 breast carcinoma tumor in vitro and in vivo. Tumour Biol. 2015 Nov;36(11):8499-510

CAIndexNames:

Phenol, 2-methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]-

SMILES:

OC1=CC(/C=C\C2=CC(OC)=C(OC)C(OC)=C2)=CC=C1OC

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