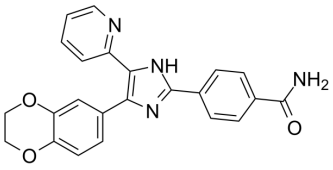
D4476

Cat. No.:	HY-10324
CAS No.:	301836-43-1
Molecular Formula:	$C_{23}H_{18}N_4O_3$
Molecular Weight:	398.41
Target:	Casein Kinase; Autophagy; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Stem Cell/Wnt; Autophagy; Apoptosis
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 : ≥ 50 mg/mL (125.50 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5100 mL	12.5499 mL	25.0998 mL
5 mM	0.5020 mL	2.5100 mL	5.0200 mL
10 mM	0.2510 mL	1.2550 mL	2.5100 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: ≥ 2.5 mg/mL (6.27 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.27 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.27 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	D4476 is a potent, selective and cell-permeable inhibitor of casein kinase 1(CK1) with an IC_{50} value of 0.3 μM in vitro.
IC_{50} & Target	CK1 0.3 μM (IC_{50})
In Vitro	D4476 is a potent and rather selective inhibitor of CK1 in vitro and in cells. In H4IIE hepatoma cells, D4476 specifically

inhibits the phosphorylation of endogenous forkhead box transcription factor O1a (FOXO1a) on Ser322 and Ser325 within its MPD, without affecting the phosphorylation of other sites. CK1δ assayed at 0.1 mM ATP using a phosphorylated peptide TFRPRTSpSNASTIS corresponding to residues 312–325 of FOXO1a is inhibited with an IC_{50} value of 0.3 μM. The IC_{50} value for CK1δ decreases progressively as the concentration of ATP is lowered, indicating that D4476 is an ATP-competitive inhibitor of CK1. CK1[1].

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

PROTOCOL

Cell Assay [2]

D4476 is used for inhibition of Csnk1a1. D4476 is added to leukemia cells cultured in 96-well plates (5,000 cells per well) in medium supplemented with 10 ng/mL mIL-3. A D4476 dose titration is performed by adding 2.5 μM, 5 μM, 10 μM, 20 μM, and 40 μM D4476 to cell cultures in a final DMSO percentage of 0.4%. Similarly, D4476 is added to LSK cells cultured in SFEM medium supplemented with mTpo and mScf. The number of cells after 96 h of treatment is assessed with CountBright absolute counting beads using flow cytometry[2].

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

CUSTOMER VALIDATION

- Nat Commun. 2021 Sep 10;12(1):5386.
- Cancers (Basel). 2021 Jul 12;13(14):3477.
- Biochem Biophys Res Commun. 2020 Apr 2;524(2):280-287.

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REFERENCES

[1]. Rena G, et al. D4476, a cell-permeant inhibitor of CK1, suppresses the site-specific phosphorylation and nuclear exclusion of FOXO1a. EMBO Rep. 2004 Jan;5(1):60-5.

[2]. Järås M, et al. Csnk1a1 inhibition has p53-dependent therapeutic efficacy?in?acute myeloid leukemia. J Exp Med.?2014 Apr 7;211(4):605-12.?

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