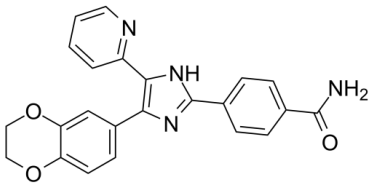
Data Sheet

Product Name:	D4476
Cat. No.:	CS-1080
CAS No.:	301836-43-1
Molecular Formula:	C23H18N4O3
Molecular Weight:	398.41
Target:	Apoptosis; Autophagy; Casein Kinase
Pathway:	Apoptosis; Autophagy; Cell Cycle/DNA Damage; Stem Cell/Wnt
Solubility:	DMSO : ≥ 50 mg/mL (125.50 mM)



BIOLOGICAL ACTIVITY:

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. IC50 & Target: IC50: 0.3 μM (CK1)[1] **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].

PROTOCOL (Extracted from published papers and Only for reference)

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].

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.?

CAIndexNames:

Benzamide, 4-[4-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-(2-pyridinyl)-1H-imidazol-2-yl]-

SMILES:

O=C(N)C1=CC=C(C=C1)C(N2)=NC(C3=CC=C4OCCOC4=C3)=C2C5=NC=CC=C5

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

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