Small Molecules

D4476

Activin/NODAL/TGF-β pathway inhibitor; Inhibits CK1, ALK5 and p38 MAPK

Catalog #	74012	5 mg
	74014	10 mg

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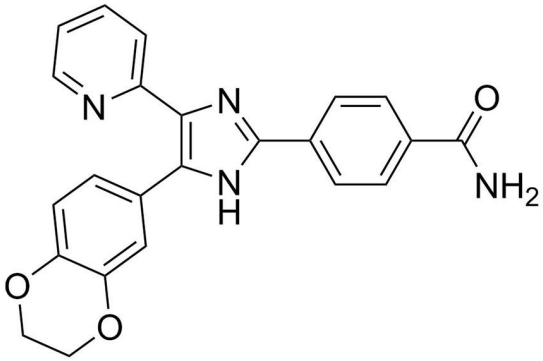
Product Description

D4476 is a selective, potent, and cell-permeant inhibitor of casein kinase (CK) 1 (Rena et al.). It inhibits CK1 and CK1δ from S. pombe (IC_{50} = 200 and 300 nM, respectively; Bain et al.; Rena et al.). It also inhibits transforming growth factor β1 (TGF-β1) type I receptor (ALK5) with IC_{50} = 500 nM (Rena et al.).

Molecular Name:	D4476
Alternative Names:	Casein Kinase I Inhibitor
CAS Number:	301836-43-1
Chemical Formula:	$C_{23}H_{18}N_4O_3$
Molecular Weight:	398.4 g/mol
Purity:	≥ 98%
Chemical Name:	4-[4-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-(2-pyridinyl)1H-imidazol-2-yl]-benzamide
Structure:	

Properties

Physical Appearance:	A crystalline solid
Storage:	Product stable at -20°C as supplied. Protect product from prolonged exposure to light. For long-term storage store with a desiccant. Stable as supplied for 12 months from date of receipt.
Solubility:	· DMSO ≤ 75 mM · Absolute ethanol ≤ 25 mM For example, to prepare a 10 mM stock solution in DMSO, resuspend 1 mg in 251 µL of DMSO. Prepare stock solution fresh before use. Information regarding stability of small molecules in solution has rarely been reported, however, as a general guide we recommend storage in DMSO at -20°C. Aliquot into working volumes to avoid repeated freeze-thaw cycles. The effect of storage of stock solution on compound performance should be tested for each application. Compound has low solubility in aqueous media. For use as a cell culture supplement, stock solution should be diluted into culture medium immediately before use. Avoid final DMSO concentration above 0.1% due to potential cell toxicity.

Published Applications

REPROGRAMMING
· Along with Forskolin (Catalog #72112) and 2-methyl-5-hydroxytryptamine, reprograms mouse somatic cells into pluripotent cells by acting as a chemical substitute for OCT4 (Hou et al.).
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CANCER RESEARCH
· Induces apoptosis of multiple myeloma cell lines (Hu et al.).
· Exhibits anti-leukemic activity by selectively killing leukemia stem cells over normal hematopoietic stem and progenitor cells (Järås et al.).

References

Bain J et al. (2003) The specificities of protein kinase inhibitors: an update. Biochem J 371(1): 199–204.
Hou P et al. (2013) Pluripotent stem cells induced from mouse somatic cells by small-molecule compounds. Science 341(6146): 651–4.
Hu Y et al. (2015) CSNK1α1 mediates malignant plasma cell survival. Leukemia 29(2): 474–82.
Järås M et al. (2014) Csnk1a1 inhibition has p53-dependent therapeutic efficacy in acute myeloid leukemia. J Exp Med 211(4): 605–12.
Rena G et al. (2004) D4476, a cell-permeant inhibitor of CK1, suppresses the site-specific phosphorylation and nuclear exclusion of FOXO1a. EMBO Rep 5(1): 60–5.

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