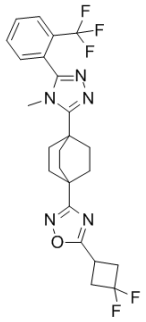
MK-4101

Cat. No.:	HY-100036
CAS No.:	935273-79-3
Molecular Formula:	$C_{24}H_{24}F_5N_5O$
Molecular Weight:	493.47
Target:	Smo; Apoptosis; Hedgehog
Pathway:	Stem Cell/Wnt; 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 (101.32 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0265 mL	10.1323 mL	20.2647 mL
5 mM	0.4053 mL	2.0265 mL	4.0529 mL
10 mM	0.2026 mL	1.0132 mL	2.0265 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 (5.07 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.07 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.07 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MK-4101 is a Smoothened (SMO) antagonist (IC_{50} of 1.1 μM for 293 cells) and also a potent inhibitor of the hedgehog pathway (IC_{50} of 1.5 μM for mouse cells; IC_{50} of 1 μM for KYSE180 oesophageal cancer cells). MK-4101 has robust antitumor activity that inhibits tumor cell proliferation and induces extensive apoptosis[1].

IC_{50} & Target

IC50: 1.1 μM (293 cells); 1.5 μM (mouse cells); 1 μM (KYSE180 oesophageal cancer cells)[1]

In Vitro

MK-4101 inhibits Hh signaling both in a reporter gene assay in an engineered mouse cell line with an IC_{50} of 1.5 μM, and in human KYSE180 oesophageal cancer cells with an IC_{50} of 1 μM. MK-4101 displaces a fluorescently-labeled cyclopamine derivative from 293 cells expressing recombinant human SMO with an IC_{50} of 1.1 μM, implying that the compound binds to SMO. MK4101 also inhibits the proliferation of medulloblastoma cells derived from neonatallyirradiated $Ptch1^{-/+}$ mice in vitro with an IC_{50} of 0.3 μM[1].

MK-4101 (10 μM; 60 hours, 72 hours; medulloblastoma or BCC cells) treatment shows cell cycle arrest with a nearly complete disappearance of the S phase subpopulation, a prominent increase of the G1 population and, to a minor extent, of the G2 population[1].

MK-4101 (10 μM; medulloblastoma or BCC cells) treatment significantly reduces cyclin D1 protein and accumulation of cyclin B1 protein[1].

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

Cell Cycle Analysis[1]

Cell Line:	Medulloblastoma or BCC cells
Concentration:	10 μM
Incubation Time:	60 hours, 72 hours
Result:	Showed cell cycle arrest.

Western Blot Analysis[1]

Cell Line:	Medulloblastoma or BCC cells
Concentration:	10 μM
Incubation Time:	
Result:	Significant reduction of cyclin D1 protein and accumulation of cyclin B1 protein.

In Vivo

MK-4101 (40-80 mg/kg; oral administration; for 3.5 weeks; CD1 nude female mice) treatment shows tumor growth inhibition (40 and 80 mg/kg) and tumor regression at the highest dose (80 mg/kg). MK-4101 treatment shows a dose-dependent down-regulation of Gli1 mRNA. The maximum effect for tumor inhibition and hedgehog pathway downregulation is achieved at 80 mg/kg[1].

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

Animal Model:	5-weeks old CD1 nude female mice with medulloblastoma/BCC cells[1]
Dosage:	40 or 80 mg/kg once a day, 80 mg/kg twice a day
Administration:	Oral administration; for 3.5 weeks
Result:	Showed tumor growth inhibition (40 and 80 mg/kg) and tumor regression at the highest dose (80 mg/kg).

REFERENCES

[1]. Filocamo G et al. MK-4101, a Potent Inhibitor of the Hedgehog Pathway, Is Highly Active against Medulloblastoma and Basal Cell Carcinoma.Mol Cancer Ther. 2016 Jun;15(6):1177-89.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA