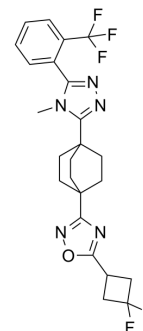


MK-4101

Cat. No.:	HY-100036		
CAS No.:	935273-79-3		
Molecular Formula:	C ₂₄ H ₂₄ F ₅ N ₅ O		
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	2 years
		-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (101.32 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		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

- 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
- 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
- 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 (IC₅₀ of 1.1 μM for 293 cells) and also a potent inhibitor of the hedgehog pathway (IC₅₀ of 1.5 μM for mouse cells; IC₅₀ of 1 μM for KYSE180 oesophageal cancer cells). MK-4101 has robust antitumor activity that inhibits tumor cell proliferation and induces extensive apoptosis^[1].

IC₅₀ & 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 IC₅₀ of 1.5 μM, and in human KYSE180 oesophageal cancer cells with an IC₅₀ of 1 μM. MK-4101 displaces a fluorescently-labeled cyclopamine derivative from 293 cells expressing recombinant human SMO with an IC₅₀ of 1.1 μM, implying that the compound binds to SMO. MK4101 also inhibits the proliferation of medulloblastoma cells derived from neonatally irradiated Ptch1^{+/+} mice in vitro with an IC₅₀ 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