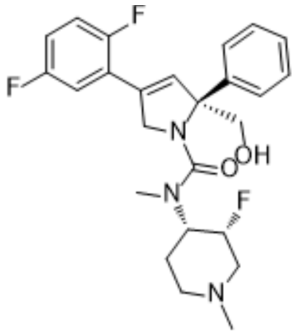
MK-0731

Cat. No.:	HY-50672
CAS No.:	845256-65-7
Molecular Formula:	$C_{25}H_{28}F_3N_3O_2$
Molecular Weight:	459.5
Target:	Kinesin; Apoptosis; Lipoxygenase
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton; Apoptosis; Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

MK-0731 is a selective, non-competitive and allosteric kinesin spindle protein (KSP) inhibitor with an IC_{50} of 2.2 nM and a pK_a of 7.6. MK-0731 is >20,000 fold selectivity against other kinesins. MK-0731 induces mitotic arrest and induces apoptosis in tumors. MK-0731 provides significant antitumor efficacy[1][2].

IC_{50} & Target

KSP
2.2 nM (IC_{50})

In Vitro

MK-0731 (0.415-300 nM; 48 h) induces apoptosis in A2780 cells with an EC_{50} of 2.7 nM[1].
MK-0731 displays little affinity for binding to the hERG channel (IC_{50}=20.5 μM)[1].
MK-0731 has the ability to induce a mitotic block with an IC_{50} of 19 nM in cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	A2780 cells
Concentration:	0.415-300 nM
Incubation Time:	48 h
Result:	Induced apoptosis with an EC_{50} of 2.7 nM.

In Vivo

MK-0731 (40 mg/kg/day; sc; for 11 days) inhibits the growth of KB-v tumors that highly overexpress Pgp, whereas Paclitaxel (HY-B0015) has no effect[1].
MK-0731 (2.5, 5, 10, 20, and 40 mg/kg/day; minipump) exhibits a dose-proportional increase in both exposure and mitotic arrest in tumors in A2780-xenografted mice[1].
MK-0731 (1 mg/kg/day; iv) has a $T_{1/2}$ of 1 hours, a CL of 66 mL/min•kg, and a V_{ss} of 3 L/kg for rats[1].
Pharmacokinetic Parameters of MK-0731 in rats[1].

	rat iv (1 mg/kg)	dog iv (0.4 mg/kg)	rhesus iv (0.4 mg/kg)
$T_{1/2}$ (h)	1	2	1

CL (mL/min/kg)	66.7	15.1	23.1
V_{ss} (L/kg)	3.0	1.6	2.3

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

Animal Model:	Mice for the dual flank xenograft KB-3-1 and KB-v-1 cells[1]
Dosage:	40 mpk
Administration:	SC; qd×1; for 11 days
Result:	Inhibited the growth of KB-v tumors that highly overexpress Pgp, whereas Paclitaxel (20 mpk; qd×5) had no effect.

REFERENCES

[1]. Christopher D Cox, et al. Kinesin spindle protein (KSP) inhibitors. 9. Discovery of (2S)-4-(2,5-difluorophenyl)-n-[(3R,4S)-3-fluoro-1-methylpiperidin-4-yl]-2-(hydroxymethyl)-N-methyl-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxamide (MK-0731) for the treatment of taxane-refractory cancer. J Med Chem. 2008 Jul 24;51(14):4239-52.

[2]. Kyle Holen, et al. A phase I trial of MK-0731, a kinesin spindle protein (KSP) inhibitor, in patients with solid tumors. Invest New Drugs. 2012 Jun;30(3):1088-95.

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