CCT 137690

Cat. No.: HY-10804

CAS No.: 1095382-05-0

Molecular Formula: $C_{26}H_{31}BrN_8O$

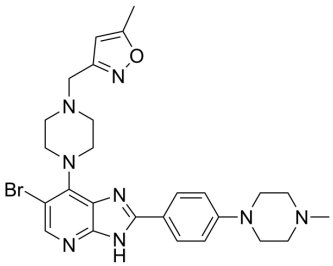
Molecular Weight: 551

Target: Aurora Kinase; Apoptosis

Pathway: Cell Cycle/DNA Damage; Epigenetics; 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 : 16.67 mg/mL (30.25 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8149 mL	9.0744 mL	18.1488 mL
5 mM	0.3630 mL	1.8149 mL	3.6298 mL
10 mM	0.1815 mL	0.9074 mL	1.8149 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: ≥ 1.67 mg/mL (3.03 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.67 mg/mL (3.03 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (3.03 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CCT 137690 is a potent and orally available aurora kinase inhibitor with IC_{50}s of 15, 25, and 19 nM for aurora A, B and C, respectively.

IC_{50} & Target

Aurora A	Aurora B	Aurora C
15 nM (IC_{50})	25 nM (IC_{50})	19 nM (IC_{50})

In Vitro

CCT 137690 displays antiproliferative activity in a range of human tumor cell lines, including SW620 colon carcinoma (GI_{50}

	=0.30 μM) and A2780 ovarian cancer cell line (GI_{50}=0.14 μM). CCT 137690 inhibits in vitro phosphorylation of histone H3. CCT 137690 is a moderate inhibitor of the hERG ion-channel (IC_{50}=3.0 μM)[1]. CCT137690 efficiently inhibits histone H3 and TACC3 phosphorylation (Aurora B and Aurora A substrates, respectively) in HCT116 and HeLa cells. Continuous exposure of tumour cells to the inhibitor causes multipolar spindle formation, chromosome misalignment, polyploidy and apoptosis[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	CCT 137690 slows the growth of the SW620 xenografts with no observed toxicity[1]. CCT 137690 significantly inhibits tumour growth in a transgenic mouse model of neuroblastoma (TH-MYCN) that overexpresses MYCN protein and is predisposed to spontaneous neuroblastoma formation[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Cells are plated in 96-well plates at 3,000 cells per well and are treated with a range of 0 to 25 mol/L of CCT137690 for 72 h. Cell proliferation assays are performed by colorimetric 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) [2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice: Animals are randomized into two groups, group 1: treatment with 100 mg/kg CCT137690 n=4 or group 2: vehicle control n=4. Treatment is administered via oral gavage twice daily. Tumour volumes are measured at day 0, 3 (48 hours after treatment started), 7 and 10 using ^{1}H MRI[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Bavetsias V, et al. Imidazo[4,5-b]pyridine derivatives as inhibitors of Aurora kinases: lead optimization studies toward the identification of an orally bioavailable preclinical development candidate. J Med Chem. 2010 Jul 22;53(14):5213-28.

[2]. Faisal A, et al. The aurora kinase inhibitor CCT137690 downregulates MYCN and sensitizes MYCN-amplified neuroblastoma in vivo. Mol Cancer Ther. 2011 Nov;10(11):2115-23.

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