(S)-Crizotinib

Cat. No.: HY-100549

CAS No.: 1374356-45-2

Molecular Formula: $C_{21}H_{22}Cl_2FN_5O$

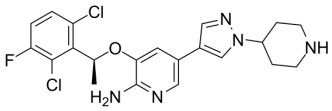
Molecular Weight: 450.34

Target: DNA/RNA Synthesis; Apoptosis

Pathway: Cell Cycle/DNA Damage; 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 : 12.5 mg/mL (27.76 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2205 mL	11.1027 mL	22.2054 mL
	5 mM	0.4441 mL	2.2205 mL	4.4411 mL
	10 mM	0.2221 mL	1.1103 mL	2.2205 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: ≥ 1.25 mg/mL (2.78 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (2.78 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (2.78 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

(S)-Crizotinib is a potent and selective MTH1 (mutT homologue) inhibitor with an IC_{50} of 330 nM. (S)-Crizotinib disrupts nucleotide pool homeostasis via MTH1 inhibition, induces an increase in DNA single strand breaks, activates DNA repair in human colon carcinoma cells, and effectively suppresses tumour growth in animal models[1].

IC_{50} & Target

IC50: 330 nM (MTH1)[1]

In Vitro

(S)-crizotinib (0.625-80 μM; 24 hours) decreases the viability of NCI-H460, H1975 and A549 cells with IC_{50} values of 14.29,

16.54 and 11.25 μM, respectively[2].
(S)-crizotinib (10-30 μM; 24 hours) induces NCI-H460, H1975 and A549 cells apoptosis[2].
(S)-crizotinib (10-30 μM; 24 hours) decreases Bcl-2: Bax ratio. (S)-crizotinib decreases B cell lymphoma 2 (Bcl-2), and Bcl-2 associated protein x (Bax) is either unaltered (H460 cells) or shows an increase (H1975 cells)[2].
(S)-Crizotinib induces apoptosis in human non-small cell lung cancer (NSCLC) cells by activating ROS-dependent ER stress apoptotic pathway independent of mutT homologue (MTH1)[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	NSCLC cells, NCI-H460, H1975 and A549 cells
Concentration:	0.625, 1.25, 2.5, 5, 10, 20, 40, 60, 80 μM
Incubation Time:	24 hours
Result:	Decreased the viability of NCI-H460, H1975 and A549 cells with IC_{50} values of 14.29, 16.54 and 11.25 μM, respectively.

Apoptosis Analysis[2]

Cell Line:	NSCLC cells, NCI-H460, H1975 and A549 cells
Concentration:	10, 20 or 30 μM
Incubation Time:	24 hours
Result:	Induced cells apoptosis.

Western Blot Analysis[2]

Cell Line:	NSCLC cells, NCI-H460, H1975 and A549 cells
Concentration:	10, 20 or 30 μM
Incubation Time:	24 hours
Result:	Decreased Bcl-2: Bax ratio.

In Vivo

(S)-crizotinib (7.5 or 15 mg/kg; intraperitoneal injections; once daily for 10 days) results in significant reductions in both tumor volume and tumor weight[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Five-week-old, athymic BALB/c nu/nu female mice (17-19 g) with NCI-H460 cells[2]
Dosage:	7.5 or 15 mg/kg
Administration:	Intraperitoneal injections; once daily for 10 days
Result:	Resulted in significant reductions in both tumor volume and tumor weight.

REFERENCES

[1]. Huber KV, et al. Stereospecific targeting of MTH1 by (S)-crizotinib as an anticancer strategy. Nature. 2014 Apr 10;508(7495):222-7.

[2]. Dai X, et al. (S)-crizotinib induces apoptosis in human non-small cell lung cancer cells by activating ROS independent of MTH1. J Exp Clin Cancer Res. 2017 Sep

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