Skp2 inhibitor 1

Cat. No.: HY-149293

CAS No.: 2760612-63-1

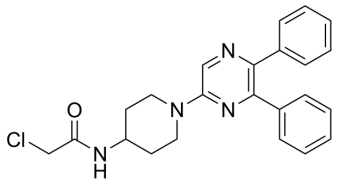
Molecular Formula: $C_{23}H_{23}ClN_4O$

Molecular Weight: 406.91

Target: E1/E2/E3 Enzyme

Pathway: Metabolic Enzyme/Protease

Storage: 4°C, sealed storage, away from moisture and light
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (122.88 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4575 mL	12.2877 mL	24.5755 mL
	5 mM	0.4915 mL	2.4575 mL	4.9151 mL
	10 mM	0.2458 mL	1.2288 mL	2.4575 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Skp2 inhibitor 1 (compound 14i) is a potent and selective Skp2 inhibitor against the Skp2-Cks1 interaction with an IC_{50} of 2.8 μM. Skp inhibitor 1 exhibits anticancer activity[1].

IC_{50} & Target

Growth arrest-specific protein 6(Gas6)-Cell Cyclin Kinase Subunit 1(Cks1) [1]IC50⊠2.8 μM(Growth arrest-specific protein 6,Gas6; Cell Cyclin Kinase Subunit 1,Cks1)[1]

In Vitro

Skp2 inhibitor 1 (2.8 μM,72 h) interferes the Skp2−Cks1 interaction, against PC-3 and MGC-803 cells with IC_{50} values of 4.8 and 7.0 μM, respectively[1].
Skp2 inhibitor 1 (10 μM, 48h) inhibits the proliferation and migration of PC-3 and MGC-803 cell, causing them to block in the S phase and promote cell apoptosis [1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	PC-3 , MGC-803
Concentration:	0-10 μM

Incubation Time:	72 h
Result:	Against the Skp2−Cks1 interaction with an IC_{50} value of 2.8 μM, and against PC-3 and MGC-803 cells with IC_{50} values of 4.8 and 7.0 μM, respectively.

Apoptosis Analysis[1]

Cell Line:	PC-3 , MGC-803
Concentration:	2.5 μM , 5 μM , 10 μM
Incubation Time:	0-48 h
Result:	Leaded to cell cycle S-phase arrest in a dose-dependent manner, and induced apoptosis in a dose-dependent manner, such as nuclear fragmentation, condensation, and cell shrinkage.

Cell Proliferation Assay[1]

Cell Line:	PC-3 , MGC-803
Concentration:	0.5 μM , 1 μM , 2 μM
Incubation Time:	10 days
Result:	Inhibited colony-forming abilities in a dose-dependent manner.

Cell Migration Assay [1]

Cell Line:	PC-3 , MGC-803
Concentration:	2.5 μM , 5 μM , 10 μM
Incubation Time:	48 h
Result:	Inhibited migration in a dose-dependent manner.

Cell Invasion Assay[1]

Cell Line:	PC-3 , MGC-803
Concentration:	0.5 μM , 1 μM , 2 μM
Incubation Time:	48 h
Result:	Inhibited invasion in a dose-dependent manner.

Western Blot Analysis[1]

Cell Line:	PC-3 , MGC-803
Concentration:	2.5 μM , 5 μM , 10 μM
Incubation Time:	0-48 h
Result:	Inhibited the protein levels of Skp2 in a dose-dependent manner, restored the expression of p21 and p27 in a time-dependent manner.

In Vivo	Skp2 inhibitor 1 (50 mg/kg, intraperitoneal injection/2 day, 21 days) inhibits tumor growth significantly in NOD-SCID

xenograft models without obvious toxicity. In addition, the tumor treated with Skp2 inhibitor 1 (50 mg/Kg/2 day) was completely suppressed in vivo[1].

Skp2 inhibitor 1 decreases tumor malignancy via suppressing the Skp2 signal pathway and increase the proportion of apoptosis in the tumor tissue[1].

Pharmacokinetic Parameters of Compound 14i in the Plasma and Tumor Tissue[1]

□□□□□□□□[1]

PK parameters	plasma	tumor tissue
$t_{1/2}$	14.1±1.5(h)	12.6±7.8(h)
Cmax	176.1±30.3(ng/mL)	182.0±80.9(ng/g)
AUC_{last}	3231.5±407.2(h.ng/mL)	2443.9±474.9(h.ng/g)
AUC_{INF}	3551.5±465.3(h.ng/mL)	2636.0±619.7(h.ng/g)
V_Z	143.3±9.2(L/kg)	170.8±80.1(mg/kg)
CL	7.1±0.8(L/h/kg)	15.7±4.2(mg/h/kg)
MRT_{last}	13.4±0.64(h)	9.9±2.5(h)

$t_{1/2}$ of 14i in the Liver Microsomes and Liver S9 ofDifferent Species[1]

□□□□□□□[1]

	species	human	rat	mouse
$t_{1/2}$	liver microsomes	66.0	16.3	15.3
$t_{1/2}$	liver S9	64.8	15.4	16.5

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

Animal Model:	The xenograft models of PC-3 and MGC-803 cells in NOD-SCID mice[1].
Dosage:	10 mg/kg; 25 mg/kg, 50 mg/kg
Administration:	Intraperitoneal injection (i.p.)
Result:	Inhibited tumor growth without obvious toxicity, the tumor growth inhibition ratio was 55.68, 71.86, and 90.42% with 10, 25, and 50 mg/Kg/2 day, respectively.

REFERENCES

[1]. Zhang K, et al. Discovery of Novel 1,3-Diphenylpyrazine Derivatives as Potent S-Phase Kinase-Associated Protein 2 (Skp2) Inhibitors for the Treatment of Cancer. J Med

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