CDK4/6-IN-14

Cat. No.: HY-151898

CAS No.: 2699091-15-9

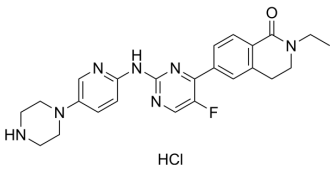
Molecular Formula: $C_{24}H_{27}ClFN_7O$

Molecular Weight: 483.97

Target: CDK

Pathway: Cell Cycle/DNA Damage

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

CDK4/6-IN-14 is a potent and highly selective CDK4 and CDK6 (CDK) inhibitor with IC_{50}s of 10 nM and 16 nM, respectively. CDK4/6-IN-14 exhibits more than 60-fold selectivity over CDKs 1, 2, 7, and 9, and shows high selectivity among other 205 kinases[1].

IC_{50} & Target

CDK4 10 nM (IC_{50})	CDK6 16 nM (IC_{50})	CDK1 >10000 nM (IC_{50})	CDK2 1045 nM (IC_{50})
CDK7 2595 nM (IC_{50})	CDK9 2664 nM (IC_{50})		

In Vitro

CDK4/6-IN-14 (compound 42; 1-6 μM; 5 days) exhibits potent inhibitory activity against the proliferation of breast cancer MCF-7, T47D, and ZR-75-1 cell lines. CDK4/6-IN-14 significantly inhibits growth and clone formation of MCF-7 and T47D cells [1].

CDK4/6-IN-14 (compound 42; 1-6 μM) arrests the cell cycle at the G1 phase of MCF-7 and T47D cells in the dose-dependent manner[1].

CDK4/6-IN-14 (compound 42; 1-6 μM; 24 hours) significantly inhibits the phosphorylation of retinoblastoma (RB), while the expression of RB protein was almost unchanged. In addition, CDK4/6-IN-14 exhibits a concentration-dependent effect to decrease the level of c-MYC and cyclin D1[1].

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

Cell Cytotoxicity Assay[1]

Cell Line:	MCF-7 and T47D cells
Concentration:	1 μM, 2 μM, 4 μM (T47D cells); 1.5 μM, 3 μM, 6 μM (MCF-7 cells)
Incubation Time:	5 days
Result:	Significantly inhibited growth and clone formation of MCF-7 and T47D cells.

Western Blot Analysis[1]

Cell Line:	MCF-7 and T47D cells
Concentration:	1 μM, 2 μM, 4 μM (T47D cells); 1.5 μM, 3 μM, 6 μM (MCF-7 cells)

Incubation Time:	24 hours
Result:	Significantly inhibited the phosphorylation of RB.

In Vivo

CDK4/6-IN-14 (compound 42; 100-150 mg/kg; p.o; once a day; for 23 days) significantly inhibits tumor growth of the MCF-7 xenograft model[1].

CDK4/6-IN-14 (compound 42) exhibits a suitable t1/2 of intravenous and oral administration (2.62 and 3.59 h, respectively). Moreover, the oral bioavailability of CDK4/6-IN-14 is 43%[1].

Pharmacokinetic Parameters of CDK4/6-IN-14 (Compound 42) in Sprague–Dawley Rats[1].

admin.	C_{max} (ng/mL)	$AUC_{0-\infty}$ (h × ng/mL)	$MRT_{0-\infty}$ (h)	T_{max} (h)	$t_{1/2}$ (h)	F (%)
IV	290.52	372.56	3.50	0.033	2.62	
PO	144.11	1612.18	9.11	6	3.59	43

Dose: i.v. at 1 mg/kg; p.o. at 10 mg/kg[1]

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

Animal Model:	BALB/c nude mice bearing MCF-7 cells[1]
Dosage:	100 mg/kg, 150 mg/kg
Administration:	Orally administertion; once a day; for 23 days
Result:	Significantly inhibited tumor growth of the MCF-7 xenograft model.

REFERENCES

[1]. Weijiao Chen, et al. Discovery, Optimization, and Evaluation of Selective CDK4/6 Inhibitors for the Treatment of Breast Cancer. J Med Chem. 2022 Nov 24;65(22):15102-15122.

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