CDK4/6-IN-15

Cat. No.: HY-142076

CAS No.: 2078047-99-9

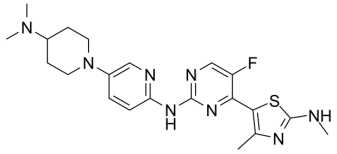
Molecular Formula: $C_{21}H_{27}FN_8S$

Molecular Weight: 442.56

Target: CDK

Pathway: Cell Cycle/DNA Damage

Storage: 4°C, protect from light
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 5 mg/mL (11.30 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2596 mL	11.2979 mL	22.5958 mL
	5 mM	0.4519 mL	2.2596 mL	4.5192 mL
	10 mM	0.2260 mL	1.1298 mL	2.2596 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 0.5 mg/mL (1.13 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CDK4/6-IN-15 is an orally active and selective CDK4/6 inhibitor. CDK4/6-IN-15 potently inhibits cancer cells growth. CDK4/6-IN-15 arrests cell cycle at G1 phase and suppresses retinoblastoma tumour suppressor protein (Rb) phosphorylation at S780 and E2 factor (E2F)-regulated gene expression[1].

IC_{50} & Target

CDK4	CDK6	CDK2
3 nM (IC_{50})	0.279 μM (IC_{50})	3.335 μM (IC_{50})

In Vitro

CDK4/6-IN-15 (compound 91) (10 μM; 24 h) also potently inhibits FLT3 and MYLK4 with inhibition rates >90%[1].
CDK4/6-IN-15 (0-5 μM; 72 h) suppresses tumour cell proliferation selectively with GI_{50}s of 0.107 μM (MV4-11) and 0.325 μM (MDA-MB-453)[1].
CDK4/6-IN-15 (0.1-1 μM; 24 h) arrests exclusively the cell cycle at G1 phase in Rb-positive MV4-11 cells and MDA-MB-453 cells [1].
CDK4/6-IN-15 (0.1-1 μM or 0.3-3 μM; 24-96 h) triggers apoptosis in MV4-11 and MDA-MB-453 cells[1].
CDK4/6-IN-15 (0.1-3.3 μM; 4-24 h) inhibits phosphorylation of Rb[1].

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

Apoptosis Analysis[1]

Cell Line:	MV4-11 and MDA-MB-453 cells
Concentration:	0.1 μM, 0.5 μM, and 1 μM for MV4-11; 0.3 μM, 0.6 μM, and 3.3 μM for MDA-MB-453 cells
Incubation Time:	24 h, 48 h, 72 h, and 96 h
Result:	Induced cell apoptosis via arresting cell cycle at G1 accompanied with Rb) phosphorylation suppression and E2F-regulated gene expression decreases.

Western Blot Analysis[1]

Cell Line:	MV4-11 (GI_{50}=0.107 μM) and MDA-MB-453 (GI_{50}=0.325 μM)
Concentration:	1×, 5×, 10× GI_{50}
Incubation Time:	4 h, 12 h, and 24 h
Result:	Resulted inhibition of Rb phosphorylation at S780.

In Vivo

CDK4/6-IN-15 (compound 91) (2 mg/kg for i.v. or 10 mg/kg for p.o.; single dose) shows comparable oral absorption in healthy male adult BALB/c mice (20-25 g) as well as (5 mg/kg for i.v. or 200 mg/kg for p.o.; single dose) in male albino Wistar rats (250-350 g)[1].

Pharmacokinetic Analysis[1]

	Route	Dose (mg/kg)	CL (mL/min/kg)	V_{ss} (L/kg)	AUC (μM·h)	C_{max} (μM)	T_{max} (h)	$t_{1/2}$ (h)	F (%)
rat	IV	5	155	27.5	1.2	1.4	/	2.1	/
	PO	20	/	/	4.4	0.3	4.3	20.3	95
mouse	IV	2	90	15.7	0.7	1.3	/	2.9	/
	PO	10	/	/	4.3	0.6	2.5	2.7	129

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REFERENCES

[1]. Tadesse S, et al. Discovery and pharmacological characterization of a novel series of highly selective inhibitors of cyclin-dependent kinases 4 and 6 as anticancer agents. Br J Pharmacol. 2018 Jun;175(12):2399-2413.

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