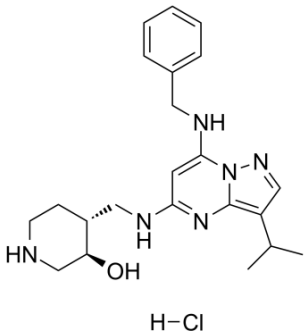
Samuraciclib hydrochloride

Cat. No.:	HY-103712A
CAS No.:	1805789-54-1
Molecular Formula:	$C_{22}H_{31}ClN_6O$
Molecular Weight:	430.97
Target:	CDK; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Apoptosis
Storage:	4°C, stored under nitrogen, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : 55 mg/mL (127.62 mM; Need ultrasonic)
DMSO : 25 mg/mL (58.01 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass	1 mg	5 mg	10 mg
1 mM	2.3203 mL	11.6017 mL	23.2035 mL
5 mM	0.4641 mL	2.3203 mL	4.6407 mL
10 mM	0.2320 mL	1.1602 mL	2.3203 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: ≥ 2.5 mg/mL (5.80 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.80 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.80 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Samuraciclib hydrochloride (CT7001 hydrochloride) is a potent, selective, ATP-competitive and orally active CDK7 inhibitor, with an IC_{50} of 41 nM. Samuraciclib hydrochloride displays 45-, 15-, 230- and 30-fold selectivity over CDK1, CDK2 (IC_{50} of 578 nM), CDK5 and CDK9, respectively. Samuraciclib hydrochloride inhibits the growth of breast cancer cell lines with GI_{50} values between 0.2-0.3 μM. Samuraciclib hydrochloride has anti-tumor effects[1][2].

IC_{50} & Target				
	CDK7/cyclin H 41 nM (IC_{50})	cdk2/cyclin A 578 nM (IC_{50})	CDK1/cyc A 1.8 μM (IC_{50})	CDK4/Cyc D1 49 μM (IC_{50})

	CDK5/p35NCK 9.4 μM (IC_{50})	CDK6/cycD1 34 μM (IC_{50})	CDK9/CycT1 1.2 μM (IC_{50})

In Vitro

Samuraciclib (ICEC0942; 0-10 μM; 24 hours; HCT116 cells) treatment promotes cell apoptosis[1].
Samuraciclib (ICEC0942; 0-10 μM; 24 hours; HCT116 cells) treatment induces cell cycle arrest[1].
Samuraciclib (ICEC0942; 0-10 μM; 0-24 hours; HCT116 cells) treatment inhibits the phosphorylation of PolII CTD in a dose and time dependent manner in HCT116 colon cancer cells. ICEC0942 also inhibits phosphorylation of CDK1, CDK2 and retinoblastoma[1].
Samuraciclib (ICEC0942) inhibits the growth of MCF7, T47D, MDA-MB-231, HS578T, MDA-MB-468, MCF10A and HMEC cells with GI_{50} values of 0.18 μM, 0.32 μM, 0. 33 μM, 0.21 μM, 0.22 μM, 0.67 μM and 1.25 μM, respectively[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	HCT116 cells
Concentration:	0 μM, 0.1 μM, 1 μM and 10 μM
Incubation Time:	24 hours
Result:	Induced caspase 3/7 and demonstrated PARP cleavage.

Cell Cycle Analysis[1]

Cell Line:	HCT116 cells
Concentration:	0 μM, 0.01 μM, 0.1 μM, 1 μM and 10 μM
Incubation Time:	24 hours
Result:	Showed accumulation of cells in G2/M.

Western Blot Analysis[1]

Cell Line:	HCT116 cells
Concentration:	0 μM, 0.1 μM, 1 μM and 10 μM
Incubation Time:	0 hour, 4 hours, 8 hours, 16 hours or 24 hours
Result:	PolII CTD phosphorylation was inhibited in a dose and time dependent manner in HCT116 colon cancer cells.

In Vivo

Samuraciclib (ICEC0942; 100 mg/kg; oral gavage; daily; for 14 days; female nu/nu-BALB/c athymic nude mice) treatment inhibits tumor growth by 60% at day 14, and is accompanied by highly significant reductions in PolII Ser2 and Ser5 phosphorylation in PBMCs and in tumors[1].
The combination of Samuraciclib (ICEC0942) and ICI 47699 treatment shows complete growth arrest of estrogen receptor (ER)-positive tumor xenografts[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female nu/nu-BALB/c athymic nude mice (7-week old) with MCF7 cells[1]
Dosage:	100 mg/kg
Administration:	Oral gavage; daily; for 14 days
Result:	At day 14, tumor growth was inhibited by 60%.

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2019 Jun 25;116(26):12986-12995.
- Cell Death Dis. 2019 Aug 9;10(8):602.

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REFERENCES

[1]. Hazel P, et al. Inhibitor Selectivity for Cyclin-Dependent Kinase 7: A Structural, Thermodynamic, and Modelling Study. ChemMedChem. 2017 Mar 7;12(5):372-380.

[2]. Patel H, et al. ICEC0942, an Orally Bioavailable Selective Inhibitor of CDK7 for Cancer Treatment. Mol Cancer Ther. 2018 Jun;17(6):1156-1166.

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