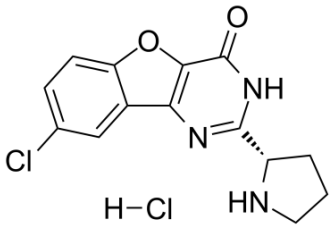
XL413 hydrochloride

Cat. No.:	HY-15260A
CAS No.:	2062200-97-7
Molecular Formula:	$C_{14}H_{13}Cl_2N_3O_2$
Molecular Weight:	326.18
Target:	CDK
Pathway:	Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

H_2O : 10 mg/mL (**30.66 mM;** Need ultrasonic)
DMSO : 3.4 mg/mL (**10.42 mM;** Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.0658 mL	15.3290 mL	30.6579 mL
	5 mM	0.6132 mL	3.0658 mL	6.1316 mL
	10 mM	0.3066 mL	1.5329 mL	3.0658 mL

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

BIOLOGICAL ACTIVITY

Description

XL413 hydrochloride is a potent, selective and ATP competitive inhibitor of **Cdc7**, with an **IC_{50}** of 3.4 nM, and also shows potent effect with **IC_{50}**s of 215, 42 nM on CK2, PIM1, respectively, and an **EC_{50}** of 118 nM on pMCM.

IC_{50} & Target

Cdc7	PIM1	CK2
3.4 nM (IC_{50})	42 nM (IC_{50})	215 nM (IC_{50})

In Vitro

XL413 inhibits the cell proliferation (IC_{50} = 2685 nM), decreases cell viability (IC_{50} = 2142 nM) and elicits the caspase 3/7 activity (EC_{50} = 2288 nM) in Colo-205 cells. XL413 also significantly inhibits the anchorage-independent growth of colo-205 in soft agar (IC_{50} = 715 nM)[1]. XL413 shows cytotoxic effects on tumors, with IC_{50} of 22.9 μM in HCC1954 cells and 1.1 μM in Colo-205 cells. XL413 induces apoptosis in the Colo-205 cells, but not in HCC1954 cells. XL413 is effective DDK inhibitors in vitro, with IC_{50} of 22.7 nM. XL413 is defective in inhibiting DDK-dependent Mcm2 phosphorylation in HCC1954 cells but is effective in Colo-205 cells[2].

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

In Vivo	XL413 (100 mg/kg, p.o.) shows excellent plasma exposures in mice and possesses good PK properties. XL413 (10, 30, or 100 mg/kg, p.o.) is well tolerated at all the doses, with no significant body weight loss[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	20 ng of purified human DDK is pre-incubated with increasing concentrations of each DDK inhibitor for 5 min. Then 10 μCi (γ)-^{32}P ATP and 1.5 μM cold ATP are added in a buffer containing 50 mM Tris-HCl (pH 7.5), 10 mM $MgCl_2$, and 1 mM DTT and incubated for 30 min at 30°C. The proteins are denatured in 1X Laemmli buffer at 100°C followed by SDS-PAGE and autoradiography on HyBlot CL film. Auto-phosphorylation of DDK is used as an indicator of its kinase activity. ^{32}P-labeled bands are quantified using ImageJ and the IC_{50} values are calculated using GraphPad. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	For assays in 96 well plates 2500 cells are plated per well. After 24 hours, cells are treated with small molecule inhibitors and incubated for 72 hours at 37°C. Subsequently the cells are lysed and the ATP content is measured as an indicator of metabolically active cells using the CellTiter-Glo assay. IC_{50} values are calculated using the GraphPad software. For assays in six well plates, 100,000 cells are plated per well. After 24 hours, cells are treated with small molecule inhibitors and incubated for varying time points. Cells are trypsinized and a suspension is made in 5 mL of phosphate buffered saline. 30 μL of this suspension is mixed with 30 μL of CellTiter-Glo reagent followed by a 10-minute incubation at room temperature. Luminescence is measured using EnVision 2104 Multilabel Reader and BioTek Synergy Neo Microplate Reader. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- **Science**. 2017 Dec 1;358(6367). pii: eaan4368.
- **Am J Physiol Lung Cell Mol Physiol**. 2018 Sep 1;315(3):L360-L370.
- **Harvard Medical School LINCS LIBRARY**

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REFERENCES

[1]. Koltun ES, et al. Discovery of XL413, a potent and selective CDC7 inhibitor. Bioorg Med Chem Lett. 2012 Jun 1;22(11):3727-31.

[2]. Sasi NK, et al. The potent Cdc7-Dbf4 (DDK) kinase inhibitor XL413 has limited activity in many cancer cell lines and discovery of potential new DDK inhibitor scaffolds. PLoS One. 2014 Nov 20;9(11):e113300.

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