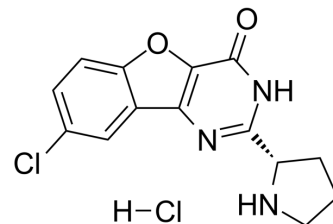


XL413 monohydrochloride

Cat. No.:	HY-15260A
CAS No.:	2062200-97-7
Molecular Formula:	C ₁₄ H ₁₃ Cl ₂ N ₃ O ₂
Molecular Weight:	326.18
Target:	CDK
Pathway:	Cell Cycle/DNA Damage
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 1 years; -20°C, 6 months (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H₂O : 10 mg/mL (30.66 mM; Need ultrasonic)
DMSO : 3.4 mg/mL (10.42 mM; Need ultrasonic and warming)

	Solvent Concentration	Mass	1 mg	5 mg	10 mg
Preparing Stock Solutions	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 (BMS-863233) hydrochloride is a potent, selective and ATP competitive inhibitor of Cdc7, with an IC₅₀ of 3.4 nM, and also shows potent effect with IC₅₀s of 215, 42 nM on CK2, PIM1, respectively, and an EC₅₀ of 118 nM on pMCM.

IC₅₀ & Target

Cdc7 3.4 nM (IC ₅₀)	PIM1 42 nM (IC ₅₀)	CK2 215 nM (IC ₅₀)
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In Vitro

XL413 (BMS-863233) hydrochloride inhibits the cell proliferation (IC₅₀=2685 nM), decreases cell viability (IC₅₀=2142 nM) and elicits the caspase 3/7 activity (EC₅₀=2288 nM) in Colo-205 cells. XL413 hydrochloride also significantly inhibits the anchorage-independent growth of colo-205 in soft agar (IC₅₀=715 nM)^[1].
XL413 hydrochloride shows cytotoxic effects on tumors, with IC₅₀ of 22.9 μM in HCC1954 cells and 1.1 μM in Colo-205 cells. XL413 hydrochloride induces apoptosis in the Colo-205 cells, but not in HCC1954 cells. XL413 is effective DDK inhibitors in vitro, with IC₅₀ of 22.7 nM. XL413 hydrochloride 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 (BMS-863233; 100 mg/kg, p.o.) hydrochloride shows excellent plasma exposures in mice and possesses good PK

properties. XL413 (10, 30, or 100 mg/kg, p.o.) hydrochloride 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 μ Ci (γ)-³²P ATP and 1.5 μ M cold ATP are added in a buffer containing 50 mM Tris-HCl (pH 7.5), 10 mM MgCl₂, 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. ³²P-labeled bands are quantified using ImageJ and the IC₅₀ 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. IC₅₀ 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 μ L of this suspension is mixed with 30 μ L 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):eaan4368.
- Sens Actuators B Chem. 15 May 2022, 131618.
- 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.

Caution: Product has not been fully validated for medical applications. For research use only.

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