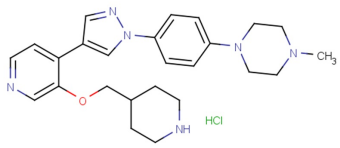
Data Sheet (Cat.No.T11996)

TargetMol
A DRUG SCREENING EXPERT

MELK-8a hydrochloride

Chemical Properties



CAS No.:	2096992-20-8
Formula:	C25H33ClN6O
Molecular Weight:	469.02
Appearance:	N/A
Storage:	0-4℃ for short term (days to weeks), or -20℃ for long term (months).

Biological Description

Description	MELK-8a hydrochloride is a novel maternal embryonic leucine zipper kinase (MELK) inhibitor.(IC50:2 nM).
Targets(IC_{50})	MELK: 2 nM
In vitro	MELK-8a is fairly soluble (0.22 g/L at pH 6.8) and shows a good permeability in the Caco-2 assay. MELK-8a inhibits the growth of MDA-MB-468 cells and MCF-7 cells with an IC50 of approximately 0.06 and 1.2 μM, respectively.MELK-8a remains very potent (IC50=140 nM) when the ATP concentration in the biochemical assay is shifted from 20 μM to 2 mM. Its potency is well tracked between full-length MELK versus catalytic domain construct (5 nM versus 2 nM). It only inhibits seven off-target kinases in addition to MELK with >85% inhibition of binding at 1 μM demonstrating great selectivity. The compound is at least 90-fold more selective in targeting MELK in all cases.
In vivo	Subcutaneous administration of MELK-8a at 30 mg/kg in C57BL/6 mice results in good plasma exposure. The compound adsorption into the systemic circulation is rapid (Tmax=0.4 h) and peak plasma concentration reaches 6.6 μM. An ascending dose PK study in female athymic nude mice shows that the rate of compound release is maximal at 120 mg/kg and all clearance mechanisms can be saturated at 240 mg/kg. However, when administered orally at 10 mg/kg in C57BL/6 male mice, it shows very poor PK (3.6% oral bioavailability) consistent with very high in vivo clearance.

Solubility Information

Solubility	H2O: 100 mg/mL (213.21 mM) DMSO: 8.6 mg/mL (18.34 mM) (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.132 mL	10.661 mL	21.321 mL
5 mM	0.426 mL	2.132 mL	4.264 mL
10 mM	0.213 mL	1.066 mL	2.132 mL
50 mM	0.043 mL	0.213 mL	0.426 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. The storage conditions and period of the stock solution: - 80 ℃ for 6 months; - 20 ℃ for 1 month. Please use it as soon as possible.

Reference

1. Touré BB, et al. Toward the Validation of Maternal Embryonic Leucine Zipper Kinase: Discovery, Optimization of Highly Potent and Selective Inhibitors, and Preliminary Biology Insight. J Med Chem. 2016 May 26;59(10):4711-23.

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