MELK-8a hydrochloride

Cat. No.: HY-100368A

CAS No.: 2096992-20-8

Molecular Formula: $C_{25}H_{33}ClN_6O$

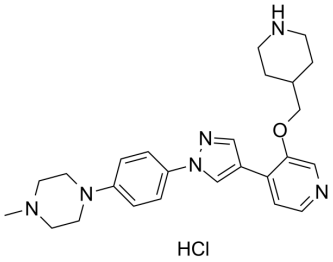
Molecular Weight: 469.02

Target: MELK

Pathway: PI3K/Akt/mTOR

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : ≥ 100 mg/mL (213.21 mM)

DMSO : 8.6 mg/mL (18.34 mM; Need ultrasonic and warming)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1321 mL	10.6605 mL	21.3211 mL
	5 mM	0.4264 mL	2.1321 mL	4.2642 mL
	10 mM	0.2132 mL	1.0661 mL	2.1321 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 50 mg/mL (106.61 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

MELK-8a hydrochloride is a novel maternal embryonic leucine zipper kinase (MELK) inhibitor with an IC_{50} of 2 nM.

IC_{50} & Target

IC50: 2 nM (MELK)[1]

In Vitro

MELK-8a remains very potent (IC_{50}=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. 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 IC_{50} of approximately 0.06 and 1.2 μM, respectively[1].

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

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 (T_{max}=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[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	MDA-MB-468 and MCF7 cells are seeded in growth medium into 96-well plates at 1000 and 4000 cells/well, respectively. Sixteen hours after plating, MELK-8a are added and incubated for 7 days. For each well, ATPLite reagent is added and incubated. Luminescence is measured on an multilabel plate reader[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: For pharmacokinetic studies, the intravenous and oral dose is prepared in a solution containing 5% ethanol, 100% PG, 5% CremophorEL, and 80% PBS. The subcutaneous dose is formulated in 10% PG and 25% (20%, v/v) Solutol. Plasma samples are collected at specified time points and stored frozen (−20 °C) until MELK-8a analysis. An LC−MS/MS method is used to quantitate MELK-8a drug levels in plasma[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Rep. 2017 Dec 5;21(10):2829-2841.
- J Biol Chem. 2020 Feb 21;295(8):2359-2374.
- School of Medicine, Department of Pharmacology. 2020 Jun.

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REFERENCES

[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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