RU-SKI 43 hydrochloride

Cat. No.: HY-18366A

CAS No.: 1782573-67-4

Molecular Formula: $C_{22}H_{31}ClN_2O_2S$

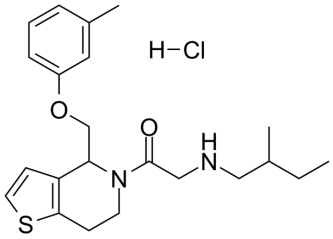
Molecular Weight: 423.01

Target: Hedgehog

Pathway: Stem Cell/Wnt

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

DMSO : ≥ 51 mg/mL (120.56 mM)

H_2O : 2.5 mg/mL (5.91 mM; Need ultrasonic)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3640 mL	11.8201 mL	23.6401 mL
5 mM	0.4728 mL	2.3640 mL	4.7280 mL
10 mM	0.2364 mL	1.1820 mL	2.3640 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 (5.91 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.91 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

RU-SKI 43 hydrochloride is a potent and selective Hedgehog acyltransferase (Hhat) inhibitor with an IC_{50} of 850 nM. RU-SKI 43 hydrochloride reduces Gli-1 activation through Smoothened-independent non-canonical signaling and decreases Akt and mTOR pathway activity. RU-SKI 43 hydrochloride has anti-cancer activity[1].

IC_{50} & Target

IC50: 850 nM (Hhat)[1]

In Vitro

RU-SKI 43 hydrochloride (10 μM; for 6 days) strongly decreases cell proliferation (83% in AsPC-1 cells) in AsPC-1 and Panc-1 cells[2].

RU-SKI 43 hydrochloride (10 or 20 μM; 5 hours) causes dose-dependent inhibition of Shh palmitoylation following only 5

hours[1].
RU-SKI 43 hydrochloride (10 μM; for 72 hours) causes a 40% decrease in Gli-1 levels in AsPC-1 cells[2].
RU-SKI 43 hydrochloride (10 μM; 48 hours) results in decreased phosphorylation (47-67%) of four proteins in the Akt pathway, including Akt (phosphorylation at both Thr307 and Ser473), PRAS40, Bad and GSK-3β. RU-SKI 43 treatment also decreases phosphorylation of mTOR and S6, members of the mTOR signaling pathway[2].
RU-SKI 43 hydrochloride behaves as an uncompetitive inhibitor (K_i=7.4 μM) with respect to Shh, and as a noncompetitive inhibitor (K_i=6.9 μM) with respect to ^{125}I-iodo-palmitoylCoA[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[2]

Cell Line:	AsPC-1 and Panc-1 pancreatic cancer cells
Concentration:	10 μM
Incubation Time:	For 6 days (drugs were replenished every 48 hours)
Result:	Strongly decreased cell proliferation (83% in AsPC-1 cells).

Western Blot Analysis[1]

Cell Line:	COS-1 cells expressing HA-Hhat and Shh
Concentration:	10 or 20 μM
Incubation Time:	5 hours
Result:	Caused dose-dependent inhibition of Shh palmitoylation following only 5 hours.

In Vivo

RU-SKI 43 hydrochloride has a $t_{1/2}$ of 17 min in mouse plasma after IV administration[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Petrova E, et al. Hedgehog acyltransferase as a target in pancreatic ductal adenocarcinoma. Oncogene. 2014 Jan 27. doi: 10.1038/onc.2013.575.

[2]. Petrova E, et al. Inhibitors of Hedgehog acyltransferase block Sonic Hedgehog signaling.Nat Chem Biol. 2013 Apr;9(4):247-9.

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