SK1-I hydrochloride

Cat. No.: HY-119016A

CAS No.: 2366222-05-9

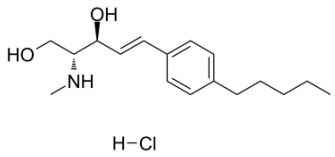
Molecular Formula: $C_{17}H_{28}ClNO_2$

Molecular Weight: 313.86

Target: SphK

Pathway: Immunology/Inflammation

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (796.53 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1861 mL	15.9307 mL	31.8613 mL
	5 mM	0.6372 mL	3.1861 mL	6.3723 mL
	10 mM	0.3186 mL	1.5931 mL	3.1861 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: ≥ 2.08 mg/mL (6.63 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.63 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (6.63 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SK1-I hydrochloride (BML-258 hydrochloride), an analog of sphingosine, is an isozyme-specific competitive SPHK1 inhibitor with a K_i value of 10 μM[1]. SK1-I hydrochloride shows no activity at SPHK1 PKCα, PKCδ, PKA, AKT1, ERK1, EGFR, CDK2, IKKβ or CamK2β. SK1-I hydrochloride enhances autophagy and has antitumor activity[2].

IC_{50} & Target

Ki: 10 μM (SPHK1)[1]

In Vitro

SK1-I hydrochloride (0-10 μM; 24 hours) attenuates cancer cell growth and survival in a TP53-dependent manner in HCT116 cells and HCT116 cells bearing TP53 null cancer[2].
SK1-I hydrochloride (0-20 μM; 12 hours) induces more CASP3 cleavage in HCT116 cells, compared to HCT116 cells lacking

TP53, leading to a hallmark of apoptosis[2].

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

Cell Viability Assay[2]

Cell Line:	HCT116 cells and HCT116 cells bearing TP53 null cancer
Concentration:	0 μM, 2.5 μM, 5 μM, 7.5 μM, 10 μM
Incubation Time:	24 hours
Result:	Decreased cancer cell growth and survival.

Western Blot Analysis[2]

Cell Line:	HCT116 cells and HCT116 cells bearing TP53 null cancer
Concentration:	0 μM, 5 μM, 10 μM, 20 μM
Incubation Time:	12 hours
Result:	Induced more CASP3 cleavage in HCT116 cells, compared to HCT116 cells lacking TP53.

In Vivo

Pre-treatment with SK1-I hydrochloride (BML-258 hydrochloride; intraperitoneal (i.p.) injection; once; 24 hours prior to baseline mean arterial blood pressure (MAP) measurement; 75 mg/kg) before anandamide (i.v. injection; two doses; 1 and 10 mg/kg) significantly decreases the hypotensive response[3].

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Animal Model:	Male C57BL/6 mice (24 ± 3.5 g) [3]
Dosage:	75 mg/kg
Administration:	Intraperitoneal (i.p.) injection; once; 24 hours prior to baseline MAP measurement
Result:	Significantly lowered baseline mean arterial blood pressure (MAP).

REFERENCES

[1]. Melissa R Pitman, et al. Inhibitors of the sphingosine kinase pathway as potential therapeutics. Curr Cancer Drug Targets. 2010 Jun;10(4):354-67.

[2]. Santiago Lima, et al. TP53 is required for BECN1- and ATG5-dependent cell death induced by sphingosine kinase 1 inhibition. Autophagy. 2018;14(6):942-957.

[3]. Fiona H Greig, et al. Requirement for sphingosine kinase 1 in mediating phase 1 of the hypotensive response to anandamide in the anaesthetised mouse. Eur J Pharmacol. 2019 Jan 5;842:1-9.

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