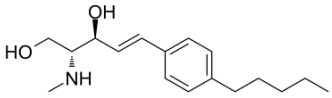
SK1-I

Cat. No.:	HY-119016
CAS No.:	1072443-89-0
Molecular Formula:	$C_{17}H_{27}NO_2$
Molecular Weight:	277.4
Target:	SPHK
Pathway:	Immunology/Inflammation
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

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

IC_{50} & Target

Ki: 10 μM (SPHK1)[1]

In Vitro

SK1-I (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 (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 (BML-258; 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.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA