上海源叶生物科技有限公司
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产品名称：SKI-178
CAS 号： 1259484-97-3
产品货号：S89211

生物活性：

Description

SKI-178 是一种有效的鞘氨醇激酶-1 (SphK1) 和 SphK2 抑制剂。SKI-178 对活性分子敏感和多药耐药癌细胞系 (如 MTR3、NCI-ADR 和 HL60/VCR) 的 IC50 浓度范围为 1.8 到 0.1 μM。SKI-178 以 CDK1 依赖性方式诱导人急性髓性白血病细胞凋亡。

IC50 & Target

SphK1　　SphK2

Cellular Effect

Cell Line	Type	Value	Description
A549	IC_{50}	0.3 μM	Cytotoxicity against human A549 cells after 48 hrs by sulforhodamine B assay
BXPC-3	IC_{50}	0.2 μM	Cytotoxicity against human BxPC3 cells after 48 hrs by sulforhodamine B assay
HL-60	IC_{50}	0.2 μM	Cytotoxicity against VCR-resistance human HL60 cells after 48 hrs by sulforhodamine B assay
HL-60	IC_{50}	0.2 μM	Cytotoxicity against human HL60 cells after 48 hrs by sulforhodamine B assay
HL-60	IC_{50}	470 nM	Cytotoxicity against human HL-60 cells assessed as reduction in cell viability after 48 hrs by MTT assay
KG-1a	IC_{50}	0.5 μM	Cytotoxicity against human KG1a cells after 48 hrs by sulforhodamine B assay
MCF7	IC_{50}	1.3 μM	Cytotoxicity against human MCF7 cells after 48 hrs by sulforhodamine B assay
MCF7	IC_{50}	1.8 μM	Cytotoxicity against human tamoxifen-resistant MCF7 cells after 48 hrs by sulforhodamine B assay
MIA PaCa-2	IC_{50}	0.1 μM	Cytotoxicity against human MIAPaCa2 cells after 48 hrs by sulforhodamine B assay
NCI-H226	IC_{50}	0.3 μM	Cytotoxicity against human NCI-H226 cells after 48 hrs by sulforhodamine B assay
NCI-H460	IC_{50}	0.3 μM	Cytotoxicity against human H460 cells after 48 hrs by sulforhodamine B assay
PANC-1	IC_{50}	0.1 μM	Cytotoxicity against human PANC1 cells after 48 hrs by sulforhodamine B assay
SH-SY5Y	IC_{50}	0.3 μM	Cytotoxicity against human SH-SY5Y cells after 48 hrs by sulforhodamine B assay
U-251	IC_{50}	0.5 μM	Cytotoxicity against human U251 cells after 48 hrs by sulforhodamine B assay
U-87MG ATCC	IC_{50}	0.6 μM	Cytotoxicity against human U87MG cells after 48 hrs by sulforhodamine B assay

In Vitro

SKI-178 (5 μM；24 小时) 诱导的凋亡细胞死亡与延长的 Bcl-2 磷酸化相关[1]。

Apoptosis Analysis[1]

Cell Line:	HL-60 cells
Concentration:	5 μM

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	Incubation Time: 24 hours Result: JNK activity (indicated by phosphorylation at Thr183/Tyr185) increased in a time-dependent manner starting as early as 2 hours continued to increase for at least 24 hours. There was a concomitant increase in apoptotic cell death indicated by the cleavage of caspase-7. Bcl-2 phosphorylation at Ser70 increased with time in response to SKI-178 treatment, reaching maximal levels at 8 hours, which was consistent with the timing of caspase-7 activation.
In Vivo	SKI-178 (20 mg/kg；异氟醚麻醉下眼眶后注射) 抑制 MLL-AF9 模型中的白血病进展[3]。 **Animal Model:** MLL-AF9 mouse model (leukemic mice)[3] **Dosage:** 20 mg/kg **Administration:** Retro-orbital injection under isoflurane anesthesia; three times per week for 1 and 3 weeks **Result:** White blood cell (WBC) counts decreased from their initial 104 cells/渭L levels and continued to decline after 3 weeks of treatment until they reached normal levels (~4×10^3 cells/μL).
Solvent&Solubility	**细胞实验:** DMSO 中的溶解度 ：50 mg/mL (126.77 mM; 超声助溶; 吸湿的 DMSO 对产品的溶解度有显著影响，请使用新开封的 DMSO）

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5354 mL	12.6768 mL	25.3537 mL
	5 mM	0.5071 mL	2.5354 mL	5.0707 mL
	10 mM	0.2535 mL	1.2677 mL	2.5354 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

动物实验：

请根据您的 实验动物和给药方式 选择适当的溶解方案。

以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用；

以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

方案 一

请依序添加每种溶剂： 10% DMSO → 40% PEG300 → 5% Tween-80 → 45% Saline

Solubility: 2.5 mg/mL (6.34 mM); 悬浊液; 超声助溶

此方案可获得 2.5 mg/mL 的均匀悬浊液，悬浊液可用于口服和腹腔注射。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；再向上述体系中加入 50 μL Tween-80，混合均匀；然后再继续加入 450 μL 生理盐水 定容至 1 mL。

生理盐水的配制：将 0.9 g 氯化钠，溶解于 ddH_2O 并定容至 100 mL，可以得到澄清透明的生理盐水

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	溶液。 方案 二 请依序添加每种溶剂： 10% DMSO → 90% Corn Oil Solubility: ≥ 2.5 mg/mL (6.34 mM); 澄清溶液 此方案可获得 ≥2.5 mg/mL（饱和度未知）的澄清溶液，此方案实验周期在半个月以上的动物实验酌情使用。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
参考文献	[1]. Hengst JA, et al. SKI-178: A Multitargeted Inhibitor of Sphingosine Kinase and Microtubule Dynamics Demonstrating Therapeutic Efficacy in Acute Myeloid Leukemia Models. Cancer Transl Med. 2017;3(4):109-121. [2]. Hengst JA, et al. Development of a sphingosine kinase 1 specific small-molecule inhibitor. Bioorg Med Chem Lett. 2010;20(24):7498-7502. [3]. Dick TE, et al. The apoptotic mechanism of action of the sphingosine kinase 1 selective inhibitor SKI-178 in human acute myeloid leukemia cell lines. J Pharmacol Exp Ther. 2015;352(3):494-508.

完整储备液配制表：

请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80° C, 6 months; -20° C, 1 month。-80° C 储存时，请在 6 个月内使用，-20° C 储存时，请在 1 个月内使用。

可选溶剂	质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg	25 mg
DMSO	**1 mM**	2.5354 mL	12.6768 mL	25.3537 mL	63.3842 mL
	5 mM	0.5071 mL	2.5354 mL	5.0707 mL	12.6768 mL
	10 mM	0.2535 mL	1.2677 mL	2.5354 mL	6.3384 mL
	15 mM	0.1690 mL	0.8451 mL	1.6902 mL	4.2256 mL
	20 mM	0.1268 mL	0.6338 mL	1.2677 mL	3.1692 mL
	25 mM	0.1014 mL	0.5071 mL	1.0141 mL	2.5354 mL
	30 mM	0.0845 mL	0.4226 mL	0.8451 mL	2.1128 mL
	40 mM	0.0634 mL	0.3169 mL	0.6338 mL	1.5846 mL
	50 mM	0.0507 mL	0.2535 mL	0.5071 mL	1.2677 mL
	60 mM	0.0423 mL	0.2113 mL	0.4226 mL	1.0564 mL
	80 mM	0.0317 mL	0.1585 mL	0.3169 mL	0.7923 mL
	100 mM	0.0254 mL	0.1268 mL	0.2535 mL	0.6338 mL