SKI II

Cat. No.: HY-13822

CAS No.: 312636-16-1

Molecular Formula: $C_{15}H_{11}ClN_2OS$

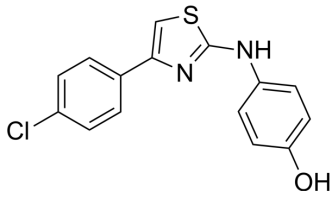
Molecular Weight: 302.78

Target: SphK; Wnt; Apoptosis

Pathway: Immunology/Inflammation; Stem Cell/Wnt; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (330.27 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.3027 mL	16.5136 mL	33.0273 mL
5 mM	0.6605 mL	3.3027 mL	6.6055 mL
10 mM	0.3303 mL	1.6514 mL	3.3027 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: ≥ 2.75 mg/mL (9.08 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.75 mg/mL (9.08 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SKI-II is an oral active and synthetic inhibitor of sphingosine kinase (SK) activity, with IC_{50} values of 78 μM and 45 μM for SK1 and for SK2, respectively. SKI II causes an irreversible inhibition of SK1 by inducing its lysosomal and/or proteasomal degradation[1][2].

IC_{50} & Target

IC50 value: 78/45 μM (SK1/2)[1][2].

In Vitro

SKI II inhibits cell proliferation by suppressing the Wnt/β-catenin signaling pathway. SKI II promotes the degradation of β-catenin by enhancing Wnt5A[1].

SKI II (1.25 μM, 48 h) in combination with DDP has a clear synergistic effect in human gastric carcinoma SGC7901/DDP cell

line[2].

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

Cell Cytotoxicity Assay[1]

Cell Line:	The human gastric carcinoma SGC7901/DDP cell line.
Concentration:	0 μM, 1.25 μM (combined with DDP).
Incubation Time:	48 hours.
Result:	SKI II in combination with DDP had a greater effect on the SGC-7901/DDP cells compared with DDP or SKI II alone.

In Vivo

Chronic SKI II (50.0 mg/kg, 3-weekly i.p. for 16 weeks) administration leads to permanent reduction of S1P concentrations in plasma in mice[3].

SKI II (50.0 mg/kg, IP; 100 mg/kg, PO) treatment reduces tumor growth in mice bearing solid tumor model[4].

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

Animal Model:	8 week-old female LDL-R$^{-/-}$ mice[3].
Dosage:	50.0 mg/kg.
Administration:	IP injection daily, 3 days a week for 16 weeks.
Result:	A single administration of produced a significant reduction of plasma S1P with themaximum (~40%) observed 12 h after injection. At sacrifice (72 h after last injection) S1P levels were 266 ± 18 ng/mL and 328 ± 30 ng/mL in the SKI-II-treated and control groups,respectively.

Animal Model:	BALB/c mouse solid tumor model that uses JC mammary adenocarcinoma cells[4].
Dosage:	50.0 mg/kg.
Administration:	IP injection daily, 3 days a week for 16 weeks.
Result:	Had strong inhibition of tumor growth from the start of treatment of 65%, with no toxicity or weight loss.

Animal Model:	BALB/c JC tumor model[4].
Dosage:	100 mg/kg.
Administration:	PO every other day.
Result:	Caused significant antitumor activity in well-established tumors as early as day 5, with maximal response seen at the end of the study. Showed 79% inhibition of tumor growth from the start of treatment.

CUSTOMER VALIDATION

- Cell Biol Int. 2020 Dec 10.

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REFERENCES

[1]. Liu H, et al. SphK1 inhibitor SKI II inhibits the proliferation of human hepatoma HepG2 cells via the Wnt5A/β-catenin signaling pathway. Life Sci. 2016 Apr 15;151:23-9.

[2]. Liu Y, et al. SKI-II reverses the chemoresistance of SGC7901/DDP gastric cancer cells. Oncol Lett. 2014 Jul;8(1):367-373.

[3]. Potì F, et al. SKI-II--a sphingosine kinase 1 inhibitor--exacerbates atherosclerosis in low-density lipoprotein receptor-deficient (LDL-R-/-) mice on high cholesterol diet. Atherosclerosis. 2015 May;240(1):212-5.

[4]. French KJ, et al. Antitumor activity of sphingosine kinase inhibitors. J Pharmacol Exp Ther. 2006 Aug;318(2):596-603.

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