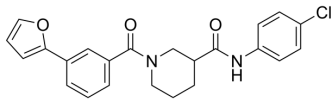
CCG-203971

Cat. No.:	HY-108361
CAS No.:	1443437-74-8
Molecular Formula:	$C_{23}H_{21}ClN_2O_3$
Molecular Weight:	408.88
Target:	Ras
Pathway:	GPCR/G Protein; MAPK/ERK Pathway
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (611.43 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4457 mL	12.2285 mL	24.4571 mL
	5 mM	0.4891 mL	2.4457 mL	4.8914 mL
	10 mM	0.2446 mL	1.2229 mL	2.4457 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (6.11 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (5.09 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.09 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CCG-203971 is a second-generation Rho/MRTF/SRF pathway inhibitor. CCG-203971 potently targets RhoA/C-activated SRE-luciferase (IC_{50} =6.4 μM). CCG-203971 inhibits PC-3 cell migration with an IC_{50} of 4.2 μM. Potential anti-metastasis Agent[1][2].

IC_{50} & Target

RhoA/MRTF-A[1]

In Vitro

CCG-203971, a second-generation Ras homolog gene family, member A (RhoA)/myocardin-related transcription factor A (MRTF-A)/serum response factor (SRF) pathway inhibitor, represses both matrix-stiffness and transforming growth factor

	beta–mediated fibrogenesis as determined by protein and gene expression in a dose-dependent manner. CCG-203971 significantly represses TGF-β- induced MKL1 expression at 25 μM concentration[2]. Human dermal fibroblasts are plated onto 96-well plates and allowed to grow for 3 days in the presence of 30 μM CCG-203971 or DMSO vehicle. Viable cell density is assessed through enzymatic reduction of the water-soluble tetrazolium dye WST-1. Scleroderma dermal fibroblasts proliferate faster than normal cells, and this is inhibited by CCG-203971[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	CCG-203971 is tested in a Bleomycin skin injury model. Bleomycin is administered in 50 μL of DMSO intraperitoneally. Preliminary studies show that Bleomycin administered in this manner is well tolerated at 100 mg/kg twice a day. Intradermal Bleomycin for 2 weeks along with the DMSO control (50 μL i.p.) results in marked dermal thickening ($P<0.0001$) compared with the PBS+DMSO group, which does not receive Bleomycin. CCG-203971 treatment strongly and significantly ($P<0.001$) suppresses the Bleomycin-induced skin thickening in this model. Skin collagen amounts, assessed by measurement of hydroxyproline content, show similar results. Bleomycin injections promote collagen deposition ($P<0.01$) and CCG-203971 is able to block this effect ($P<0.05$)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	Human dermal fibroblasts (2.0×10^4) are plated into a 96-well plate and grown overnight in DMEM containing 10% FBS. Media are removed and replaced with DMEM containing 2% FBS and 30 μM CCG-203971 or 0.1% DMSO control. After 72 hours WST-1 dye is added to each well, and after 60 minutes absorbance at 490 nm is read using a Wallac Victor2 plate reader[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice[3] Skin fibrosis is induced in C57BL/6 mice (female, 8 weeks old) by local intracutaneous injection of 100 μL of Bleomycin (1 mg/mL) in phosphate-buffered saline (PBS), every day for 2 weeks in a defined area (~1 cm^2) on the upper back. Intracutaneous injection of 100 μL of PBS is used as a control. Three groups of mice with a total of 21 mice are used. One group receives injections of PBS and the other two are challenged with Bleomycin. Twice-a-day intraperitoneal administration of CCG-203971 (100 mg/kg in 50 μL of DMSO) is initiated together with the first challenge of Bleomycin and continues for 2 weeks. DMSO is used as the vehicle control. The three groups of animals are: (1) PBS/DMSO; (2) Bleomycin/DMSO; and (3) Bleomycin/CCG-203971. After treatment, animals are humanely killed by cervical dislocation, and tissue is collected[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Johnson LA, et al. Novel Rho/MRTF/SRF inhibitors block matrix-stiffness and TGF-β-induced fibrogenesis in human colonic myofibroblasts. Inflamm Bowel Dis. 2014 Jan;20(1):154-65.

[2]. Haak AJ, et al. Targeting the myofibroblast genetic switch: inhibitors of myocardin-related transcription factor/serum response factor-regulated gene transcription prevent fibrosis in a murine model of skin injury. J Pharmacol Exp Ther. 2014 Jun;349(3):480-6.

[3]. Bell JL, et al. Optimization of novel nipecotic bis(amide) inhibitors of the Rho/MKL1/SRF transcriptional pathway as potential anti-metastasis agents. Bioorg Med Chem Lett. 2013 Jul 1;23(13):3826-32.

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

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