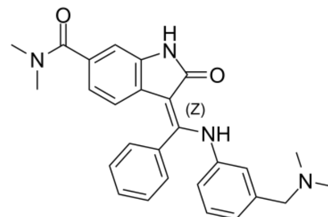
MCE® MedChemExpress

Product Data Sheet

Inhibitors • Agonists • Screening Libraries

BIX02189

Cat. No.:	HY-12056
CAS No.:	1265916-41-3
Molecular Formula:	$C_{27}H_{28}N_4O_2$
Molecular Weight:	440.54
Target:	MEK; ERK
Pathway:	MAPK/ERK Pathway; Stem Cell/Wnt
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 : ≥ 49.4 mg/mL (112.14 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	2.2699 mL	11.3497 mL	22.6994 mL
5 mM	0.4540 mL	2.2699 mL	4.5399 mL
10 mM	0.2270 mL	1.1350 mL	2.2699 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: ≥ 2.5 mg/mL (5.67 mM); Clear solution
2. Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
   Solubility: ≥ 2.5 mg/mL (5.67 mM); Clear solution
3. Add each solvent one by one: **10% DMSO >> 90% corn oil**
   Solubility: ≥ 2.5 mg/mL (5.67 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BIX02189 is a potent and selective **MEK5** inhibitor with an **IC_{50}** of 1.5 nM. BIX02189 also inhibits **ERK5** catalytic activity with an **IC_{50}** of 59 nM.

IC_{50} & Target

MEK5	ERK5	CSF1R (FMS)	LCK
1.5 nM (IC_{50})	59 nM (IC_{50})	46 nM (IC_{50})	250 nM (IC_{50})

	JAK3 440 nM (IC_{50})	TGFβR1 580 nM (IC_{50})	RPS6KA6 (RSK4) 990 nM (IC_{50})	RPS6KA3 (RSK2) 2.1 μM (IC_{50})
	FGFR1 1 μM (IC_{50})	KIT 1.1 μM (IC_{50})	ABL1 2.4 μM (IC_{50})	MAPK14 (p38 alpha) 3.7 μM (IC_{50})
	SRC 7.6 μM (IC_{50})			

In Vitro	BIX02189 blocks phosphorylation of ERK5, without affecting phosphorylation of ERK1/2 in sorbitol-stimulated HeLa cells. BIX02189 inhibits ERK5 phosphorylation in a dose dependent manner[1]. Fluvastatin reduces advanced glycation endproduct (AGE)-induced vascular smooth muscle cells (VSMCs) proliferation. To confirm this effect, VSMCs are treated with AGEs in the presence or absence of Fluvastatin and then subject to MTT assay. AGEs are found to dose-dependently induce cell proliferation, and this is significantly suppressed by Fluvastatin. In addition to MTT assay, the similar results are got with cell counting. This suppressive effect of Fluvastatin is prevented when VSMCs are pretreated with BIX02189. Whether ERK5 activation can reduce proliferation is also examined by using Ad-CA-MEK5α encoding a constitutively active mutant form of MEK5α (an upstream kinase of ERK5). AGE-induced proliferation determined by both MTT assay and cell counting is significantly diminished in the presence of Ad-CA-MEK5α, and Nrf2 depletion using siRNA restored AGE-induced proliferation[2].
In Vivo	Mice are treated with either 10 mg/kg of BIX02189 (in 25% DMSO) or vehicle control (same volume of 25% DMSO) by intraperitoneal injection. The nuclear localization of Nrf2 is inhibited in aortic endothelial cells from mice treated with BIX02189[3].

PROTOCOL

Cell Assay [2]	AGE-induced proliferation is quantified using the MTT assay. Briefly, **VSMCs** are cultured on 24-well plates and when ~80% confluent, medium is replaced with serum free DMEM. Cells are then pretreated with **BIX02189 (2 μM)** and stimulated with Fluvastatin (5 μM) for 24 h. MTT reagents are added for 4 h at 37°C the removed by washing with PBS, and eluted with DMSO. Proliferation is measured using a microplate reader at 570 nm[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice[3] **C57BL/6-specific pathogen-free mice** are used. To determine the role of ERK5 on laminar flow-dependent Nrf2 nuclear translocation in vivo, 6-week-old male C57BL/6 mice are intraperitoneally treated with **BIX02189** (**10 mg/kg** of body weight in 25% DMSO) or vehicle control. Following euthanization, vascular perfusion is performed with saline for 5 min followed by fixation with 4% paraformaldehyde for 5 min. Isolated aorta is incubated with 0.1% PBS with Tween, and then fat is removed. 5% goat serum is used for blocking and antibody diluents. Aortic endothelial cells are stained with anti-vascular endothelial-cadherin antibody and Topro3 for endothelial cell junction and nuclear, respectively. Cellular localization of Nrf2 is determined by immunofluorescence staining with anti-Nrf2 antibody under the Confocal microscope[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- **Stem Cell Reports**. 2018 Oct 9;11(4):929-943.
- **Harvard Medical School LINCS LIBRARY**

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Tatake RJ, et al. Identification of pharmacological inhibitors of the MEK5/ERK5 pathway. Biochem Biophys Res Commun. 2008 Dec 5;377(1):120-5.

[2]. Hwang AR, et al. Fluvastatin inhibits AGE-induced cell proliferation and migration via an ERK5-dependent Nrf2 pathway in vascular smooth muscle cells. PLoS One. 2017 May 22;12(5):e0178278.

[3]. Kim M, et al. Laminar flow activation of ERK5 protein in vascular endothelium leads to atheroprotective effect via NF-E2-related factor 2 (Nrf2) activation. J Biol Chem. 2012 Nov 23;287(48):40722-31.

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