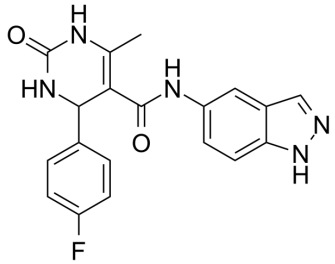
GSK180736A

Cat. No.:	HY-18990
CAS No.:	817194-38-0
Molecular Formula:	$C_{19}H_{16}FN_5O_2$
Molecular Weight:	365.36
Target:	ROCK
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton; Stem Cell/Wnt; TGF-beta/Smad
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 : ≥ 30 mg/mL (82.11 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7370 mL	13.6851 mL	27.3703 mL
5 mM	0.5474 mL	2.7370 mL	5.4741 mL
10 mM	0.2737 mL	1.3685 mL	2.7370 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 (6.84 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.84 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.84 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK180736A is potent Rho-associated coiled-coil kinase 1 (ROCK1) inhibitor with an IC_{50} of 100 nM. GSK180736A is also a selective and ATP-competitive G protein-coupled receptor kinase 2 (GRK2) inhibitor with an IC_{50} of 0.77 μM.

IC_{50} & Target

ROCK1	GRK2
100 nM (IC_{50})	770 nM (IC_{50})

In Vitro	GSK180736A is a compound structurally similar to paroxetine that is developed as a ROCK inhibitor, is shown to be an even more potent and selective inhibitor of GRK2 with an IC_{50} of 0.77 μM and more than 100-fold selectivity over other GRKs. ROCK1 is a potential therapeutic target in the treatment of cardiovascular diseases such as hypertension. GSK180736A is a weak inhibitor of PKA with an IC_{50} of 30 μM, but highly potent against ROCK1 (IC_{50}=100 nM)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cardiac myocytes are isolated from LV free wall and septum of C57/Bl6 mice. Cells are treated with isoproterenol (0.5 μM) for 2 min for the recording of contraction, with pretreatment of either PBS as vehicle or paroxetine (10 μM), 215022 (0.1, 0.5, 1, 10 μM), 215023 (0.1, 0.5, 1, 10 μM), 224064 (0.1, 0.5, 1, 10 μM), and GSK180736A (0.5, 1 μM), for 10 min[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Acta Pharm Sin B. 2021 Jan 23.
- Clin Sci (Lond). 2020 Feb 14;134(3):331-347.
- Cells. 2019 Dec 8;8(12):1596.
- SSRN. 2019 May.

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REFERENCES

[1]. Waldschmidt HV, et al. Structure-Based Design, Synthesis, and Biological Evaluation of Highly Selective and Potent G Protein-Coupled Receptor Kinase 2 Inhibitors. J Med Chem. 2016 Apr 28;59(8):3793-807.

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