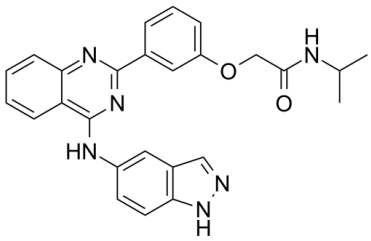
Data Sheet

Product Name:	SLx-2119
Cat. No.:	CS-0776
CAS No.:	911417-87-3
Molecular Formula:	C26H24N6O2
Molecular Weight:	452.51
Target:	ROCK
Pathway:	Cell Cycle/DNA Damage; Stem Cell/Wnt; TGF-beta/Smad
Solubility:	DMSO : ≥ 29 mg/mL (64.09 mM); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

SLx-2119 (KD-025) is a selective inhibitor of **ROCK2** with an **IC_{50}** of 105 nM. IC50 & Target: IC50: 105 nM (ROCK2)[1] **In Vitro:** SLx-2119 (40 μM) induces significant down-regulations of Tsp-1 and CTGF mRNA levels in PASMC. The microarray hybridized with aRNA from HMVEC treated with SLx-2119, shows a 5-times higher background than the other arrays[1]. **In Vivo:** SLx-2119 (KD-025; 100, 200 or 300 mg/kg, i.p.) dose-dependently reduces infarct volume after transient middle cerebral artery occlusion. SLx-2119 is at least as efficacious in aged, diabetic or female mice, as in normal adult males[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [1]Western blots are used to determine whether HMVEC, NHDF and PASMC express ROCK1 and ROCK2. The cells are incubated for 24 hours in 3 mL culture media containing SLx-2119. All cells are collected at passage 3 and lysed on ice in 25 mM Tris-HCl pH 7.5, 150 mM NaCl, 0.5% tritonX-100, 10% glycerol, 10 mM NaF and a protease inhibitor cocktail. Protein concentration is determined using a BCA protein assay reagent. Cell lysates (35 μg) are separated on 7.5% or 12.5% SDS-PAGE polyacrylamide gels and transferred to PVDF membrane filters. Membranes are blocked in 5% non-fat milk in TBS containing 0.1% Tween 20. Blots are probed with antibodies to ROCK1, ROCK2 or actin and washed well before incubation with HRP-conjugated secondary antibodies and visualization with an enhanced chemiluminescence (ECL) kit. **Animal Administration:** [2]Young adult (C57BL/6, 2-3 months old, male 22-30 g, female 16-23 g), aged (C57BL/6, 12 months old, 33-52 g) are used in all experiments. Vehicle (0.4% methylcellulose) or SLx-2119 (100, 200 or 300 mg/kg) is administered every 12 h via orogastric gavage. The dosing paradigm is chosen based on the pharmacokinetic profile after oral administration in mice. Atorvastatin (4 mg/mL) is dissolved in phosphate-buffered saline (pH 7.4) containing 45% 3-hydroxypropyl-B-cyclodextrin and 10% ethanol, and administered at a dose of 20 mg/kg per day as a single daily intraperitoneal injection for 2 weeks..

References:

[1]. Boerma, M., et al. Comparative gene expression profiling in three primary human cell lines after treatment with a novel inhibitor of Rho kinase or atorvastatin. Blood Coagul Fibrinolysis, 2008. 19(7): p. 709-18.

[2]. Lee, J.H., et al. Selective ROCK2 Inhibition In Focal Cerebral Ischemia. Ann Clin Transl Neurol, 2014. 1(1): p. 2-14.

[3]. Yang W, et al. Critical role of ROCK2 activity in facilitating mucosal $CD4^+$ T cell activation in inflammatory bowel disease. J Autoimmun. 2018 May;89:125-138.

[4]. Chen W, et al. Screening RhoA/ROCK inhibitors for the ability to prevent chronic rejection of mouse cardiac allografts.Transpl Immunol. 2018 Jun 6. pii:

S0966-3274(18)30029-7.

CAIndexNames:

Acetamide, 2-[3-[4-(1H-indazol-5-ylamino)-2-quinazolinyl]phenoxy]-N-(1-methylethyl)-

SMILES:

O=C(NC(C)C)COC1=CC=CC(C2=NC(NC3=CC4=C(NN=C4)C=C3)=C5C=CC=CC5=N2)=C1

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