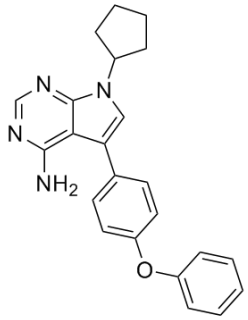
RK-24466

Cat. No.:	HY-108318
CAS No.:	213743-31-8
Molecular Formula:	$C_{23}H_{22}N_4O$
Molecular Weight:	370.45
Target:	Src
Pathway:	Protein Tyrosine Kinase/RTK
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 : 45 mg/mL (121.47 mM; Need ultrasonic)
H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6994 mL	13.4971 mL	26.9942 mL
5 mM	0.5399 mL	2.6994 mL	5.3988 mL
10 mM	0.2699 mL	1.3497 mL	2.6994 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: ≥ 2.25 mg/mL (6.07 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.25 mg/mL (6.07 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.25 mg/mL (6.07 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

RK-24466 (KIN 001-51) is a potent and selective Lck inhibitor; inhibits Lck (64-509) and LckCD isoforms with IC_{50}s of less than 1 and 2 nM, respectively.

IC_{50} & Target

IC50: <1 nM (Lck (64-509)), 2 nM (LckCD)[1]

In Vitro

RK-24466 is selective for Lck over a range of receptor, non-receptor tyrosine kinases and seronine/threonine kinases. RK-

	24466 are potent inhibitors of IL2 production in Jurkat cells stimulated with anti-CD3 antibody, being at least 100-fold more potent than PP1. RK-24466 displays remarkable cellular selectivity[1]. RK-24466 significantly inhibits both VSMC proliferation and migration. RK-24466 suppresses VSMC proliferation and migration via down-regulating the protein kinase B (Akt) and extracellular signal regulated kinase (ERK) pathways, and it significantly decreases the expression of proliferating cell nuclear antigen (PCNA) and cyclin D1 and, the phosphorylation of retinoblastoma protein (pRb)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	RK-24466 inhibits T-cell receptor stimulated (a-CD3 mAb) IL-2 production in mice at low doses (ED_{50}=4 mg/kg) after ip administration. However, efficacy is greatly reduced after oral administration (ED_{50}=25 mg/kg) which is presumed to reflect poor intestinal absorption in the latter regimen. Inhibition of antigen specific T-cell immune responses is also seen for RK-24466. After administration of RK-24466 twice daily (100 mg/kg po) for 3 days during the in vivo priming phase, a 70% inhibition of IFNγ production is seen upon subsequent antigen-specific (KLH) challenge of lymphocytes from the draining lymph nodes in vitro[3]. RK-24466 suppresses the migration of VSMCs from endothelium-removed aortic rings, as well as neointima formation following rat carotid balloon injury[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	To examine the concentration-dependent effect of the RK-24466, VSMCs are cultured in 10% FBS-supplemented DMEM containing either vehicle (DMSO 2%, v/v) or increasing concentrations of the RK-24466 (1 to 10 μM) for 24 h, and cellular proliferation is determined by using CCK-8[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Rats: For the RK-24466 treated group, RK-24466 at a final blood concentration of 5 μM is intravenously injected through femoral vein. At 14d after BI, the rats are anesthetized, and the carotid arteries are excised. The entire length of the right carotid artery is balloon injured. The left carotid artery serves as an uninjured intra-animal control. To assess the neointima formation, H&E stained section is imaged, and the intima to media thickness ratio is measured[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Arnold LD, et al. Pyrrolo[2,3-d]pyrimidines containing an extended 5-substituent as potent and selective inhibitors of lck I. Bioorg Med Chem Lett. 2000 Oct 2;10(19):2167-70.

[2]. Seo HH, et al. 7-cyclopentyl-5-(4-phenoxyphenyl)-7H-pyrrolo[2,3-d] pyrimidin-4-ylamine inhibits the proliferation and migration of vascular smooth muscle cells by suppressing ERK and Akt pathways. Eur J Pharmacol. 2017 Mar 5;798:35-42.

[3]. Burchat AF, et al. Pyrrolo[2,3-d]pyrimidines containing an extended 5-substituent as potent and selective inhibitorsof lck II. Bioorg Med Chem Lett. 2000 Oct 2;10(19):2171-4.

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