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产品名称：7-CYCLOPENTYL-5-(4-PHENOXY)PHENYL-7H-PYR
产品别名：RK-24466；KIN 001-51

生物活性：

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].
In Vivo	RK-24466 inhibits T-cell receptor stimulated (a-CD3 mAb) IL-2 production in mice at low doses (ED50=4 mg/kg) after ip administration. However, efficacy is greatly reduced after oral administration (ED50=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].
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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

	Solubility: ≥ 2.25 mg/mL (6.07 mM); Clear solution 此方案可获得 ≥ 2.25 mg/mL (6.07 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 22.5 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: 2.25 mg/mL (6.07 mM); Suspended solution; Need ultrasonic 此方案可获得 2.25 mg/mL (6.07 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 22.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.25 mg/mL (6.07 mM); Clear solution 此方案可获得 ≥ 2.25 mg/mL (6.07 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 22.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	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].
Animal Administration	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].
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.