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产品名称：RIPA-56
产品别名：RIPA-56

生物活性：

Description	RIPA-56 is a highly potent, selective, and metabolically stable inhibitor of receptor-interacting protein 1 (RIP1) with an IC_{50} of 13 nM. RIPA-56 can be used for the treatment of systemic inflammatory response syndrome[1].
IC_{50} & Target	IC50: 13 nM (RIP1)[1]
In Vitro	RIPA-56 shows efficient inhibition of RIP1 kinase activity, with an IC_{50} of 13 nM and no inhibition of RIP3 kinase activity at a 10 μM concentration. RIPA-56 also demonstrates potency in protection of murine L929 cells from TNFα/z-VAD-FMK (TZ)-induced necrosis (EC_{50}=27 nM)[1].
In Vivo	In the SIRS mice disease model, RIPA-56 efficiently reduces tumor necrosis factor alpha (TNFα)-induced mortality and multi-organ damage. Compared to known RIP1 inhibitors, RIPA-56 is potent in both human and murine cells, is much more stable in vivo, and is efficacious in animal model studies. RIPA-56 has an impressive PK profile in mice with a 3.1 h half-life, 22% oral bioavailability (P.O.), and 100% bioavailability from intraperitoneal injection (I.P.)[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (451.88 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	4.5188 mL	22.5938 mL	45.1875 mL
	5 mM	0.9038 mL	4.5188 mL	9.0375 mL
	10 mM	0.4519 mL	2.2594 mL	4.5188 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: ≥ 2.5 mg/mL (11.30 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (11.30 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 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: ≥ 2.5 mg/mL (11.30 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (11.30 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 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: ≥ 2.5 mg/mL (11.30 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (11.30 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Ren Y, et al. Discovery of a Highly Potent, Selective, and Metabolically Stable Inhibitor of Receptor-InteractingProtein 1 (RIP1) for the Treatment of Systemic Inflammatory Response Syndrome. J Med Chem. 2017 Feb 9;60(3):972-986.

实验参考：

Cell Assay	Cell necrosis assay is performed in 96-well cell culture plate. 3,000 cells are plated in each well and cultured at 37°C overnight. HT-29 cells are treated with 20 ng/mL TNFα/100 nM Smac Mimetics/20 μM z-VAD-FMK and RIPA-56 for 24 h. L929 cells are treated with 20 ng/mL TNFα/20 μM z-VAD-FMK and RIPA-56 for 6 h. The cell survival ratio is determined using the Cell Titer-Glo Luminescent Cell Viability Assay kit[1].
Animal Administration	Mice: Following intraveneous (IV), intraperitoneal (IP), or oral administration (PO) of RIPA-56 to C57BL/6 mice (n=3), blood is sampled through eye puncture at various time points. Compound concentrations in the plasma samples are analyzed by LCMS/MS. Pharmacokinetic parameters are determined from individual animal data using noncompartmental analysis in phoenix 64[1].
References	[1]. Ren Y, et al. Discovery of a Highly Potent, Selective, and Metabolically Stable Inhibitor of Receptor-InteractingProtein 1 (RIP1) for the Treatment of Systemic Inflammatory Response Syndrome. J Med Chem. 2017 Feb 9;60(3):972-986.