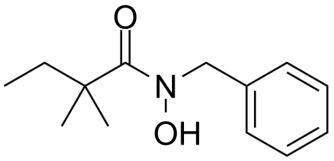
RIPA-56

Cat. No.:	HY-101032		
CAS No.:	1956370-21-0		
Molecular Formula:	$C_{13}H_{19}NO_2$		
Molecular Weight:	221.3		
Target:	RIP kinase		
Pathway:	Apoptosis		
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 : ≥ 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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.75 mg/mL (12.43 mM); Clear solution
2. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.75 mg/mL (12.43 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (11.30 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (11.30 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (11.30 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

RIPA-56 is a highly potent, selective, and metabolically stable inhibitor of receptor-interactingprotein 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Thromb Haemostasis. 2023 Sep 11.
- Stem Cells Dev. 2020 Apr 15;29(8):475-487.
- Patent. US20220362179A1.

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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.

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