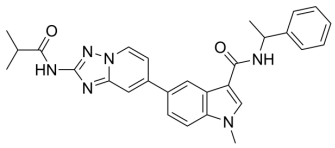
RI-962

Cat. No.:	HY-148382
CAS No.:	2763831-53-2
Molecular Formula:	$C_{28}H_{28}N_6O_2$
Molecular Weight:	480.56
Target:	RIP kinase; Necroptosis
Pathway:	Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	RI-962 is a potent and selective receptor-interacting protein kinase 1 (RIPK1) inhibitor. RI-962 inhibits RIPK1 with an IC_{50} value of 35.0 nM. RI-962 can be used for the research of nervous system diseases and inflammatory diseases[1].
IC_{50} & Target	IC50: 35.0 nM (RIPK1); EC50: 10.0 nM (HT29 cells), 4.2 nM (L929 cells), 11.4 nM (J774A.1 cells), 17.8 nM (U937 cells)[1].

In Vitro

RI-962 has potent inhibitory activity for RIPK1 with an IC_{50} value of 35.0 nM[1].
RI-962 has protective effect for necroptotic death with EC_{50} values of 10.0 nM, 4.2 nM, 11.4 nM, and 17.8 nM for HT29, L929, J774A.1, and U937 cells, respectively[1].
RI-962 (0-100 μM; 24 h) protectes cells from TSZ-induced necroptosis by inhibiting the kinase activity of RIPK1[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	HT29, L929, J774A.1, and U937 cells
Concentration:	0-100 μM
Incubation Time:	24 h
Result:	Exerted a dose-dependent protective effect against necroptotic death.

Western Blot Analysis[1]

Cell Line:	HT29 cells
Concentration:	0-400 nM
Incubation Time:	
Result:	Markedly inhibited the phosphorylation of RIPK1 and its downstream signaling proteins RIPK3 and MLKL in a dose-dependent manner.

In Vivo

RI-962 (i.p.; 40 mg/kg; once a day for 10 day) ameliorates TNFα-induced SIRS and reduces inflammation in acute DSS-induced colitis[1].
Pharmacokinetic Parameters of RI-962 in rats (i.v., i.p., p.o.; 5, 20 mg/kg) [1].

RI-962	i.v.	p.o.	i.p.
Dose (mg/kg)	5	20	20
$T_{1/2}$ (h)	2.1 ± 0.2	1.3 ± 0.2	8.5 ± 1.6
T_{max} (h)	0.1 ± 0.0	0.8 ± 1.0	0.5 ± 0.0
C_{max} (ng/mL)	12170.4 ± 1198.5	674.2 ± 424.7	3603.3 ± 693.3
AUC_{0-t}(ng*h/mL)	4526.1 ± 546.0	1594.9 ± 891.8	6459.7 ± 1131.6
$AUC_{0-\infty}$ (ng*h/mL)	4538.1 ± 546.3	1604.5 ± 896.1	6609.3 ± 1121.4
V_{ss} (L/kg)	0.4 ± 0.1	-	-
$MRT_{0-\infty}$ (h)	0.4 ± 0.0	1.8 ± 0.2	2.8 ± 0.1
CL (mL/min/kg)	18.5 ± 2.1	-	-
F (%)	-	8.8 ± 5.0	35.7 ± 6.3

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57BL/6 female mice[1]
Dosage:	40 mg/kg
Administration:	Intraperitoneal for 15 min; once a day for 10 day
Result:	Ameliorated TNFα-induced SIRS by inhibiting RIPK1 activity. Suppressed the RIPK1 signaling in the mouse model of DSS-induced colitis.

Animal Model:	Sprague-Dawley (SD) rats[1]
Dosage:	5, 20 mg/kg
Administration:	intravenous (i.v.) (5 mg/kg), intraperitoneal (i.p.) (20 mg/kg) and oral (p.o.) (20 mg/kg)
Result:	Had good metabolic stability in rats.

REFERENCES

[1]. Yueshan Li, et al. Generative deep learning enables the discovery of a potent and selective RIPK1 inhibitor. Nat Commun. 2022 Nov 12;13(1):6891.

Caution: Product has not been fully validated for medical applications. For research use only.

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