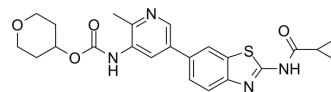


RIPK1-IN-11

Cat. No.:	HY-144276
CAS No.:	2173557-02-1
Molecular Formula:	C ₂₃ H ₂₄ N ₄ O ₄ S
Molecular Weight:	452.53
Target:	RIP kinase
Pathway:	Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	RIPK1-IN-11 is a potent and orally active RIPK1 inhibitor ($K_d=9.2$ nM; $IC_{50}=67$ nM). RIPK1-IN-11 inhibits necroptosis in both human and mouse cells ($EC_{50}=17-30$ nM). Anti-inflammatory activity ^[1] .																									
In Vitro	<p>RIPK1-IN-11 (compound 70) (24 hours; for 1h prior to the treatment of TNFα) efficiently blocks necroptosis induced by TNFα in both human and mouse cells ($EC_{50}=17-30$ nM)^[1].</p> <p>Pharmacokinetic profiles of compound 70 in male SD rats</p> <table border="1"> <thead> <tr> <th></th> <th>IV (2 mg/kg)</th> <th>PO (10 mg/kg)</th> </tr> </thead> <tbody> <tr> <td>T_{max} (h)</td> <td></td> <td>1.2</td> </tr> <tr> <td>C_{max} (ng/mL)</td> <td>1330</td> <td>1241</td> </tr> <tr> <td>AUC_{0-24} (ng/mL\timesh)</td> <td>1208</td> <td>3827</td> </tr> <tr> <td>$t_{1/2}$ (ng/mL)</td> <td>1.0</td> <td>1.7</td> </tr> <tr> <td>CL (mL/min/kg)</td> <td>33</td> <td></td> </tr> <tr> <td>Vd, ss (L/kg)</td> <td>2.4</td> <td></td> </tr> <tr> <td>F (%)</td> <td></td> <td>63%</td> </tr> </tbody> </table> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>			IV (2 mg/kg)	PO (10 mg/kg)	T_{max} (h)		1.2	C_{max} (ng/mL)	1330	1241	AUC_{0-24} (ng/mL \times h)	1208	3827	$t_{1/2}$ (ng/mL)	1.0	1.7	CL (mL/min/kg)	33		Vd, ss (L/kg)	2.4		F (%)		63%
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In Vivo	<p>RIPK1-IN-11 (3 mg/kg; i.p. for 30 min, followed by injection with TNFα) blocks hypothermia and death in mice in the TNFα-induced SIRS model^[1].</p> <p>RIPK1-IN-11 (5 mg/kg, 25 mg/kg; p.o.; 7 days; C57BL/6 mouse) exhibits no obvious toxicity in mice^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>																									

Animal Model:	C57BL/6 female mice (TNF-induced systemic inflammatory response syndrome) ^[1]
Dosage:	3 mg/kg
Administration:	i.p. for 30 min, followed by injection with TNF α (0.25 μ g/g)
Result:	Significantly reduced TNF α -induced temperature loss and ameliorated lethal shock in mice.

REFERENCES

[1]. Li Z, Hao Y, Yang C, et al. Design, synthesis, and evaluation of potent RIPK1 inhibitors with in vivo anti-inflammatory activity. *Eur J Med Chem.* 2022;228:114036.

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

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