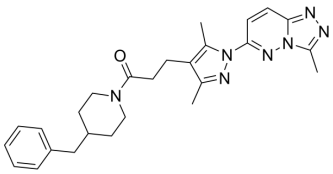
C25-140

Cat. No.:	HY-120934
CAS No.:	1358099-18-9
Molecular Formula:	$C_{26}H_{31}N_7O$
Molecular Weight:	457.57
Target:	TNF Receptor; E1/E2/E3 Enzyme
Pathway:	Apoptosis; Metabolic Enzyme/Protease
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 : 41.67 mg/mL (91.07 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1855 mL	10.9273 mL	21.8546 mL
	5 mM	0.4371 mL	2.1855 mL	4.3709 mL
	10 mM	0.2185 mL	1.0927 mL	2.1855 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.55 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.55 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.55 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

C25-140, a first-in-class, orally active, and fairly selective TRAF6-Ubc13 inhibitor, directly binds to TRAF6, and blocks the interaction of TRAF6 with Ubc13. C25-140 lowers TRAF6 activity, reduces NF-κB activation, and combats autoimmunity[1].

IC_{50} & Target

TRAF6-Ubc13[1]

In Vitro

C25-140 dose-dependently impedes TRAF6-Ubc13 interaction[1].
?C25-140 (10-30 μM; 2 hours) effectively reduces TRAF6-mediated ubiquitin chain formation[1].

?C25-140 affects TNFα-induced phosphorylation of IκBα as well as NF-κB-induced target gene expression[1].
?C25-140 efficiently inhibits IL-1β- and TNFα-mediated receptor signaling in the context of cytokine activation[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	$TRAF6_{WT}$
Concentration:	10 μM, 20 μM, 30 μM
Incubation Time:	2 hours
Result:	Effectively reduced TRAF6-mediated ubiquitin chain formation.

In Vivo

C25-140 (~1.5 mg/kg; topically to the shaved back and the right ear; twice daily for 6 days) ameliorates symptoms of autoimmune psoriasis in R 837-induced psoriasis mouse model[1].
?C25-140 (6-14 mg/kg; given i.p.; twice daily for 14 days) shows a dose-dependent improvement of RA disease outcome in Collagen-induced arthritis (CIA) model[1].
?C25-140 (10 mg/kg; i.v.) treatment shows that the C_{max}, AUC, $t_{1/2}$ and V_d are 9.7 μg/mL, 274083 ng min/mL, 80.62 min, and 4.13 L/kg, respectively[1].
.?C25-140 (10 mg/kg; p.o.) treatment shows that the C_{max}, AUC, $t_{1/2}$ and V_d are 3.4 μg/mL, 124034 ng min/mL, 127.33 min and 13.3 L/kg, respectively[1].
?C25-140 (10 mg/kg; i.p.) treatment shows that the C_{max}, AUC, $t_{1/2}$ and V_d are 4.2μg/mL, 100000 ng min/mL, 184 min, 25.6 L/kg, respectively[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	R 837-induced psoriasis mouse model (male BALB/c mice)[1]
Dosage:	~1.5 mg/kg
Administration:	Topically to the shaved back and the right ear; twice daily for 6 days
Result:	Showed a dose-dependent improvement of RA disease outcome.

Animal Model:	Collagen-induced arthritis (CIA) model in DBA1/J mice[1]
Dosage:	6 mg/kg, 10 mg/kg, 14 mg/kg
Administration:	Given i.p.; twice daily for 14 days
Result:	Ameliorated the arthritic index to almost baseline levels in this efficacy model at doses of 10 and 14 mg/kg. Dose-dependently improved symptoms of RA including inflammation and structural damage.

Animal Model:	BALB/C mice[1]
Dosage:	10 mg/kg
Administration:	I.v. (Pharmacokinetic Analysis)
Result:	The C_{max}, AUC, $t_{1/2}$ and V_d were 9.7 μg/mL, 274083 ng min/mL, 80.62 min, and 4.13 L/kg, respectively.

CUSTOMER VALIDATION

- Theranostics. 2023 Jun 26;13(11):3761-3780.
- J Neuroinflammation. 2022 Dec 22;19(1):310.
- Phytomedicine. 20 January 2022, 153952.
- Front Pharmacol. https://pubmed.ncbi.nlm.nih.gov/34489703
- Int Immunopharmacol. 2021 May 19;96:107774.

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REFERENCES

[1]. Brenke JK, et al. Targeting TRAF6 E3 ligase activity with a small-molecule inhibitor combats autoimmunity. J Biol Chem. 2018 Aug 24;293(34):13191-13203.

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