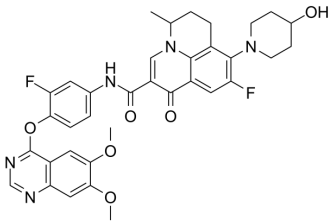
TL4830031

Cat. No.:	HY-150041
CAS No.:	2084107-15-1
Molecular Formula:	$C_{35}H_{33}F_2N_5O_6$
Molecular Weight:	657.66
Target:	TAM Receptor
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 2.38 mg/mL (3.62 mM; ultrasonic and warming and adjust pH to 5 with HCl and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5205 mL	7.6027 mL	15.2054 mL
	5 mM	---	---	---
	10 mM	---	---	---

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

BIOLOGICAL ACTIVITY

Description

TL4830031 (compound 8i), a quinolone antibiotic derivatives, is a potent Axl inhibitor with an IC_{50} value of 26 nM. TL4830031 inhibits the phosphorylation of Axl. TL4830031 inhibits cell invasion and migration. TL4830031 can be used for cancer research[1].

In Vitro

TL4830031 (compound 8i) binds to Axl with a K_d value of 1.1 nM. TL4830031 exhibits a 25 fold less potency against Mer with a K_d value of 25 nM, while it is much less potent to Tyro3 with a K_d value of 750 nM[1].

TL4830031 (0-5000 nM; 4 h; MDA-MB-231 cells) inhibits the phosphorylation of Axl (pAxl (Tyr702)) and the downstream Akt(pAkt(Thr308)) in a dose-dependent manner[1].

TL4830031 (0-5000 nM; 4 h) reverses the expression of the EMT markers induced by TGF-β1 in MDA-MB-231 cells[1].

TL4830031 (0-5000 nM; 24 h) suppresses migration and invasion of MDA-MB-231 cells[1].

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

Western Blot Analysis[1]

Cell Line:	MDA-MB-231 cells

Concentration:	0, 8, 40, 200, 1000 and 5000 nM
Incubation Time:	4 hours
Result:	Inhibited the phosphorylation of Axl (pAxl (Tyr702)) and the downstream Akt (pAkt(Thr308)) at a low concentration.

Western Blot Analysis[1]

Cell Line:	MDA-MB-231 cells
Concentration:	0, 40, 200, 1000 and 5000 nM
Incubation Time:	4 hours
Result:	Increased the expression of epithelial marker E-cadherin and decreased the expression of mesenchymal marker N-cadherin in MDA-MB-231 cells.

In Vivo

TL4830031 (compound 8i) (0-800 mg/kg; p.o.; daily, for 7 d; ICR mice) has toxicity to liver and kidney in ICR mice[1].
TL4830031 (2.5-50 mg/kg; p.o. and i.v.; SD rats) exhibits reasonable pharmacokinetic (PK) properties with an $AUC_{0-\infty}$ value of 25944.7 μg/mL·h and a $T_{1/2}$ value of 5.68 h at an oral dose of 25 mg/kg. The C_{max} (2386.9 μg/L=3.6 μM) occurred at 4.0 h postdose[1].

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

Animal Model:	ICR mice[1]
Dosage:	0, 50, 100, 200, 400, 600 and 800 mg/kg
Administration:	Oral administration; daily, for 7 days
Result:	Had toxicity to liver and kidney at 200 mg/kg, 400 mg/kg and 800 mg/kg administration.

Animal Model:	SD rats[1]
Dosage:	2.5 and 25 mg/kg
Administration:	Oral administration (2.5 mg/kg) and intravenous injection (25 mg/kg)

Result:

Administration	p.o. (25 mg/kg)	i.v. (2.5 mg/kg)
$AUC_{0-\infty}$ (μg/mL·h)	25944.7	20680.6
C_{max} (ng/mL)	2386.9	4358.2
$T_{1/2}$ (h)	5.68	4.26
T_{max} (h)	4.0	
CLz (L/h/kg)		0.12

BA (%)	12.5	

REFERENCES

[1]. Tan L, et, al. Quinolone antibiotic derivatives as new selective Axl kinase inhibitors. Eur J Med Chem. 2019 Mar 15;166:318-327.

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