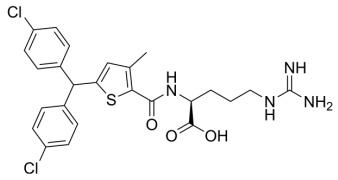
JR14a

Cat. No.:	HY-138161
CAS No.:	2411440-41-8
Molecular Formula:	$C_{25}H_{26}Cl_2N_4O_3S$
Molecular Weight:	533.47
Target:	Complement System
Pathway:	Immunology/Inflammation
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 (187.45 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8745 mL	9.3726 mL	18.7452 mL
	5 mM	0.3749 mL	1.8745 mL	3.7490 mL
	10 mM	0.1875 mL	0.9373 mL	1.8745 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: ≥ 2.5 mg/mL (4.69 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.69 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (4.69 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

JR14a is a potent thiophene antagonist of human complement C3a receptor. JR14a shows selectivity for the human C3a receptor over C5a receptor. JR14a can suppress C3aR-mediated inflammation[1].

IC_{50} & Target

human complement C3a receptor[1]

In Vitro

JR14a (0.1 nM-100 μM) inhibits C3a-induced intracellular Ca^{2+} release in human monocyte-derived macrophages, with an IC_{50} of 10 nM[1].

JR14a (0.1 nM-100 μM) is metabolically stable to exposure over 1 h to rat liver microsomes[1].
JR14a (0.1 nM-100 μM) inhibits C3a-induced β-hexosaminidase secretion in human LAD2 mast cells, with an IC_{50} of 8 nM[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

JR14a (10 mg/kg; p.o. 2 h prior) reduces paw swelling by 65% over control at 30 min after agonist injection in acute rat paw model of inflammation and edema[1].
JR14a (1 mg/kg; i.v.) exhibits elimination half-life (191 min), clearance (4.4 mL/min/kg) and AUC (3795 ng h/mL) in rats[1].
JR14a (10 mg/kg; p.o.) exhibits C_{max} (88 ng/mL), T_{max} (300 min) and AUC (478 ng h/mL) in rats[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Wister rats (8 weeks, 250-300 g) were injected with BR103[1]
Dosage:	10 mg/kg
Administration:	P.o. 2 h prior to agonist challenge
Result:	Inhibited C3aR-mediated inflammation.

Animal Model:	Male Wister rats (8 weeks, 250-300 g)[1]
Dosage:	1 mg/kg for i.v.; 10 mg/kg for oral (Pharmacokinetic Analysis)
Administration:	Intravenous administration and oral administration
Result:	I.v.: $t_{1/2}$=191 min, clearance=4.4 mL/min/kg, AUC=3795 ng•h/mL. P.o.: C_{max}=88 ng/mL, T_{max}=300 min, AUC=478 ng•h/mL.

CUSTOMER VALIDATION

- J Am Soc Nephrol. 2022 Jul 1;ASN.2021101384.

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REFERENCES

[1]. Rowley JA, et, al. Potent Thiophene Antagonists of Human Complement C3a Receptor with Anti-Inflammatory Activity. J Med Chem. 2020 Jan 23;63(2):529-541.

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