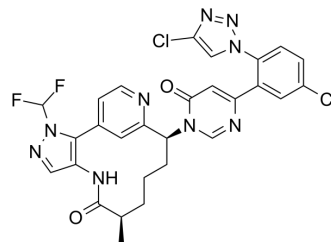


Milvexian

Cat. No.:	HY-125856		
CAS No.:	1802425-99-5		
Molecular Formula:	C ₂₈ H ₂₃ Cl ₂ F ₂ N ₉ O ₂		
Molecular Weight:	626.44		
Target:	Factor Xa		
Pathway:	Metabolic Enzyme/Protease		
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 : ≥ 100 mg/mL (159.63 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent	Mass	1 mg	5 mg	10 mg
	Concentration				
	1 mM		1.5963 mL	7.9816 mL	15.9632 mL
	5 mM		0.3193 mL	1.5963 mL	3.1926 mL
	10 mM		0.1596 mL	0.7982 mL	1.5963 mL

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

BIOLOGICAL ACTIVITY

Description

Milvexian is an orally bioavailable, small-molecule, reversible, direct antagonists of factor Xia, with the K_i of 0.11, 0.38, 0.64, 490, 350 nM for human, rabbit, dog, rat, mouse, respectively. Milvexian shows anti-thrombosis activity in vitro and in vivo, and can be used for thrombus study^[1].

In Vitro

Milvexian (10 μM, approximately) increases activated partial thromboplastin time (APTT) in human plasma, but does not alter platelet aggregation responded to ADP, arachidonic acid, and collagen in human plasma^[1].
 MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Milvexian (20 mg/kg for PO) produces average plasma concentrations of 2000 and 40 nM at 1 and 24 h after dosing, respectively^[1].
 Milvexian (0.8 mg/kg for i.v.) produces average plasma concentrations of 2000 and 100 nM at 10 min and 8 h after dosing, respectively^[1].
 Milvexian (0.063-4 + 0.04- 2.68 mg/kg for i.v. plus a continuous infusion) inhibites the formation of thrombosis in vivo^[2].

Pharmacokinetic Analysis in Rabbits^[1]

Route	Dose (mg/kg)	Clearance (mL/min/kg)	Volume of Distribution (L/kgL)	Half-life (h)	Oral Bioavailability (%)
i.v./p.o.	0.8/20	6.7	1.4	2.5	14

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

Animal Model:	The rabbit electrically mediated carotid arterial thrombosis model ^[1]
Dosage:	Prevention: 0.063 + 0.04, 0.25 + 0.17, and 1 + 0.67 (mg/kg + mg/kg/h) Treatment: 0.25 + 0.17, and 1 + 0.67 (mg/kg + mg/kg/h)
Administration:	Intravenous injection (i.v.) plus a continuous infusion
Result:	Decreased carotid blood flow(CBF) to 32-76% and reduced thrombus weight by 15-70%. Decreased CBF to 40% of control initiated after 15 min. Decreased CBF to 39-66% after Seventy-five minutes.

Animal Model:	The rabbit cuticle bleeding time model ^[1]
Dosage:	Prevention: 0.063 + 0.04, 0.25 + 0.17, and 1 + 0.67 (mg/kg + mg/kg/h) Prevention: 0.063 + 0.04, 0.25 + 0.17, and 1 + 0.67 (mg/kg + mg/kg/h) Treatment: 0.25 + 0.17, and 1 + 0.67 (mg/kg + mg/kg/h)
Administration:	Intravenous injection (i.v.) plus a continuous infusion
Result:	Did not increase the carotid blood flow(BT) with combination of Aspirin (HY-14654).

Animal Model:	The rabbit arteriovenous shunt model ^[2]
Dosage:	Prevention: 0.063 + 0.04, 0.25 + 0.17, and 1 + 0.67 (mg/kg + mg/kg/h) Prevention: 0.063 + 0.04, 0.25 + 0.17, and 1 + 0.67 (mg/kg + mg/kg/h)0.25 + 0.17, 1.0 + 0.67, and 4.0 + 2.68 mg/kg
Administration:	Intravenous injection (i.v.) plus a continuous infusion
Result:	Reduced thrombus weight of thrombosis by 34.3 -66.9 %. Increased the prolongation of APTT with 1.54-3.12-fold, but did not alter the PT and TT.

REFERENCES

- [1]. Pancras C. Wong, et al. Milvexian, an orally bioavailable, small-molecule, reversible, direct inhibitor of factor XIa: In vitro studies and in vivo evaluation in experimental thrombosis in rabbits.
- [2]. Xinkang Wang, et al. Antithrombotic Effects of the Novel Small-Molecule Factor XIa Inhibitor Milvexian in a Rabbit Arteriovenous Shunt Model of Venous Thrombosis. TH Open. 2023 Apr; 7(2): e97-e104.
- [3]. Wong P, et al. Small-Molecule Factor XIa Inhibitor, BMS-986177/JNJ-70033093, Prevents and Treats Arterial Thrombosis in Rabbits at Doses that Preserve Hemostasis [abstract]. Res Pract Thromb Haemost. 2020; 4 (Suppl 1).

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

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