FXIa-IN-8

Cat. No.: HY-144658

CAS No.: 2744293-04-5

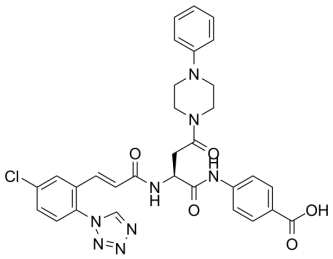
Molecular Formula: $C_{31}H_{29}ClN_8O_5$

Molecular Weight: 629.07

Target: Factor Xa

Pathway: Metabolic Enzyme/Protease

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

FXIa-IN-8 is a potent and selective FXIa inhibitor with an IC_{50} of 14.2 nM. FXIa-IN-8 shows antithrombotic activity without increasing the bleeding risk and obvious toxicitysup>[1].

IC_{50} & Target

IC_{50}: 14.2 nM (FXIa); 27900 nM (PKal)[1]

In Vitro

FXIa-IN-8 (compound 35) (0-250 μg/mL) shows significant anticoagulant activity toward the intrinsic pathway without affecting the extrinsic pathway[1].

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

In Vivo

FXIa-IN-8 shows selectivity for FXIa and PKal with IC_{50}s of 14.2, 27900 nM, respectively[1].

FXIa-IN-8 (6.5, 19.5 mg/kg; i.v.) shows antithrombotic activity in vivo[1].

FXIa-IN-8 (50, 100 mg/kg; i.v.) shows no acute toxicity[1].

FXIa-IN-8 (10 mg/kg; i.v.) shows moderate PK profiles[1].FXIa-IN-8 (19.5, 39 mg/kg) exhibits a much lower bleeding risk than heparin sodium at 300 IU/kg[1].

Pharmacokinetic Parameters of FXIa-IN-8 in Male SD rats[1].

compd 35	$T_{1/2}$ (h)	C_{max} (μg/mL)	AUC_{0-t} (h·μg/mL)	$AUC_{0-\infty}$ (h·μg/mL)	V_z(mL/kg)	Cl (mL/h/kg)	MRT_{0-t} (h)
i.v. (10 mg/kg)	1.26	57	18.3	18.4	969	553	0.32

Male SD rats; 10 mg/kg for i.v.[1].

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

Animal Model:	Male SD rats[1]
Dosage:	10 mg/kg (300 IU/kg (2.7 mg/kg) heparin sodium were injected into the tail vein 10 min before surgery)
Administration:	I.v.
Result:	Showed moderate PK profiles with a half-life value ($T^{1/2}$) of 1.26 h and a clearance (Cl)

	value of 553 mL/h/kg.

Animal Model:	C57BL/6J mice (FeCl3-induced carotid artery thrombus model)[1]
Dosage:	6.5, 19.5 mg/kg
Administration:	I.v.
Result:	Slightly prolonged the time of occlusion at 6.5 mg/kg, and showed excellent antithrombotic activity at 35 mg/kg.

Animal Model:	ICR mice[1]
Dosage:	50, 100 mg/kg
Administration:	I.v.
Result:	Showed no obvious toxic reaction to different tissues of mice.

Animal Model:	C57BL/6J mice[1]
Dosage:	19.5, 39, 20, 60, 100 mg/kg
Administration:	I.v.
Result:	Showed a low bleeding risk at 60 and 100 mg/kg.

REFERENCES

[1]. Yao N, et al. Targeting the S2 Subsite Enables the Structure-Based Discovery of Novel Highly Selective Factor XIa Inhibitors. J Med Chem. 2022; 65(5):4318-4334.

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