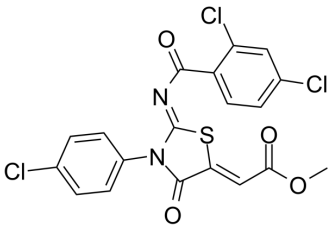
FR-171113

Cat. No.:	HY-108555
CAS No.:	173904-50-2
Molecular Formula:	$C_{19}H_{11}Cl_3N_2O_4S$
Molecular Weight:	469.73
Target:	Protease-Activated Receptor (PAR)
Pathway:	GPCR/G Protein
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

FR171113 is a specific and non-peptide thrombin receptor antagonist. FR171113 exhibits the antithrombotic effects of a PAR1 antagonist. FR171113 inhibits thrombin-induced platelet aggregation with an IC_{50} of 0.29 μM.[1][2][3][4].

In Vitro

FR171113 shows antiplatelet effect on the aggregation of guinea pig platelets induced by PAR1 agonist peptide and thrombin in vitro with IC_{50}s of 1.5 and 0.35 μM, respectively[2].
FR171113 (0.032-1 μM) dose-dependently inhibits platelet aggregation induced by both thrombin and TRAP-6[1].
FR171113 significantly prevents the plasma-elicited up-regulation of RAGE, MCP-1 and ICAM-1 mRNA levels in HUVECs[2].
FR171113 (1 μM; pretreatment for 30 minutes) inhibits thrombin- and SFLLRN (human PAR1 agonist peptide)-induced ERK activation, but not factor Xa- or SLIGKV (PAR2 agonist peptide)-induced ERK activation, indicating that activation of ERK by factor Xa is specifically mediated by PAR2 in mesangial cells[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	Human washed platelets
Concentration:	0.001, 0.01, 0.1, 1, 10, 100 μM
Incubation Time:	
Result:	The IC_{50} value for thrombin-induced platelet aggregation was 0.29 μM. The IC_{50} value for TRAP-6-induced platelet aggregation was 0.15 μM.

RT-PCR[2]

Cell Line:	human umbilical vein endothelial cells (HUVECs)
Concentration:	1 μM
Incubation Time:	4 hours
Result:	3% citrated human plasma-evoked ROS generation, RAGE, MCP-1 and ICAM-1 gene induction was significantly blocked.

Western Blot Analysis[3]

Cell Line:	Mesangial cells
Concentration:	1 μM
Incubation Time:	Pretreatment for 30 minutes
Result:	Pretreatment inhibited thrombin (10 nM; for 5 minutes)- and SFLLRN(100 μM for 5 minutes)-induced ERK activation.

In Vivo

FR171113 suppresses occlusive thrombosis dose dependently and causes significant prolongation at 1 mg/kg s.c. in the carotid artery thrombosis model.FR171113 shows antiplatelet and antithrombotic effects in vivo. FR171113 is a useful agent for investigating antithrombotic actions via PAR1 in vivo[4].

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

Animal Model:	Male Hartley guinea pigs (650–950 g) were anesthetized with urethane (1.25 g/kg, i.p.)[4]
Dosage:	0.32, 1.0, and 3.2 mg/kg
Administration:	Administered subcutaneously (s.c.)
Result:	Pretreatment with FR171113 prolonged this parameter in a dose-dependent manner. The time to thrombotic occlusion for 0.32, 1.0 and 3.2 mg/kg of FR171113 was 30.7±5.36, 44.7±8.41 and 92.6±9.79, respectively.

REFERENCES

[1]. Y Kato, et al. In vitro antiplatelet profile of FR171113, a novel non-peptide thrombin receptor antagonist. Eur J Pharmacol. 1999 Nov 19;384(2-3):197-202.

[2]. Yuji Ishibashi, et al. Advanced glycation end products potentiate citrated plasma-evoked oxidative and inflammatory reactions in endothelial cells by up-regulating protease-activated receptor-1 expression. Cardiovasc Diabetol. 2014 Mar 13;13:60.

[3]. Misa Tanaka, et al. Role of coagulation factor Xa and protease-activated receptor 2 in human mesangial cell proliferation. Kidney Int. 2005 Jun;67(6):2123-33.

[4]. Yasuko Kato, et al. Inhibition of arterial thrombosis by a protease-activated receptor 1 antagonist, FR171113, in the guinea pig. Eur J Pharmacol. 2003 Jul 25;473(2-3):163-9.

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