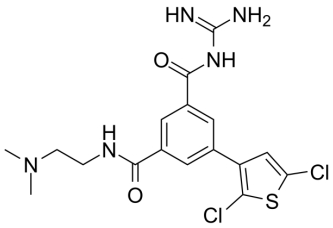
FR183998 free base

Cat. No.:	HY-100302
CAS No.:	239440-20-1
Molecular Formula:	$C_{17}H_{19}Cl_2N_5O_2S$
Molecular Weight:	428.34
Target:	Na+/H+ Exchanger (NHE)
Pathway:	Membrane Transporter/Ion Channel
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (583.65 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3346 mL	11.6730 mL	23.3459 mL
	5 mM	0.4669 mL	2.3346 mL	4.6692 mL
	10 mM	0.2335 mL	1.1673 mL	2.3346 mL

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

BIOLOGICAL ACTIVITY

Description

FR183998 free base is a potent Na^+/H^+-exchange inhibitor, with IC_{50}s of 0.3 nM, 3.1 nM and 6.5 nM by measurement of pH_i change in rat lymphocytes, rat and human platelets, respectively.

IC_{50} & Target

IC50: 0.3 nM (Na^+/H^+-exchange, Rat lymphocytes), 3.1 nM (Na^+/H^+-exchange, Human platelet), 6.5 nM (Na^+/H^+-exchange, Rat platelet)[1]

In Vitro

FR183998 free base is a Na^+/H^+-exchange inhibitor, with IC_{50}s of 0.3 nM, 6.5 nM and 3.1 nM by measurement of pH_i change in rat lymphocytes, rat and human platelets, respectively[1].

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

In Vivo

FR183998 (0.1 and 1.0 mg/kg, i.v.) shows no effect hemodynamic parameters, and does not affect mean blood pressure and heart rate in conscious rats. Pretreatment of 0.01, 0.032, 0.10 mg/kg FR183998 or posttreament of 0.032 and 0.10 mg/kg FR183998 via intravenous administration, dose-dependently reuces reperfusion-induced ventricular fibrillation (VF) and mortality in reperfusion-induced arrhythmias in anesthetized rats, with ED_{50}s against VF of 0.015 mg/kg and 0.070 mg/kg, respectively. FR183998 also reduces myocardial infarct sizes, and suppresses the arrhythmias in anesthetized rats[1]. FR183998 (1 mg/kg, i.v.) reduces the increase in serum levels of alanine transaminase, aspartate transaminase, and lactate

dehydrogenase induced by hepatic I/R, and prevents the incidences of hepatic necrosis, apoptosis, and neutrophil infiltration. FR183998 blocks the I/R-induced activation of the NF-κB, reduces induction of iNOS and inhibits the production of nitric oxide. FR183998 also decreases the expression of the iNOS gene antisense transcript in the liver of hepatic I/R rats[2] .

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PROTOCOL

Cell Assay [1]

Intracellular pH of rats lymphocytes is measured at 37°C with a spectrofluorometer by using the ratio of the emission (530 nm) obtained at 490- and 440-nm excitation wavelengths. After addition of 10 µL of the BCECF- and acid-loaded cells to 460 µL of Na-free buffer with 5 µL of DMSO or FR183998, 25 µL of 2.0 M NaCl (final 100 mM) is applied to start the reaction. The pH_i change of cells is measured for >2 min. The initial increase in pH_i in response to the added NaCl is taken as an estimate of Na^+/H^+-exchange activity, and the inhibitory effect of the drug is evaluated as IC_{50} value. The BCECF fluorescence signals are calibrated by titration with stepwise addition of small volumes of 1 M MES after permeabilization of the cells with 0.5% Triton X-100[1].

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Animal Administration [1]

Male Sprague-Dawley rats age 9-10 weeks are anesthetized with sodium pentobarbital (50 mg/kg, i.p.), intubated, and ventilated with room air at a stroke volume of 4.5 mL with a frequency of 50 strokes/min. Saline or FR183998 is injected into the left femoral vein (bolus i.v.) 5 min before occlusion. Thoracotomy for coronary artery ligation is performed at the left side of the thorax above the heart, and the origin of the left anterior descending coronary artery is occluded by applying negative tension by aspiration through polyethylene tubing connected to the vacuum system, which can achieve regional ischemia. Successful occlusion is confirmed by ischemia-induced alteration of electrocardiogram (ECG). After 5-min ischemia, reperfusion is performed, and the incidence of ventricular tachycardia (VT) and ventricular fibrillation (VF) of >5 s is observed intermittently over a 5-min period of reperfusion[1].

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REFERENCES

[1]. Ohara F, et al. Preischemic and postischemic treatment with a new Na+/H+-exchange inhibitor, FR183998, shows cardioprotective effects in rats with cardiac ischemia and reperfusion. J Cardiovasc Pharmacol. 1999 Dec;34(6):848-56.

[2]. Ishizaki M, et al. Protective effect of FR183998, a Na+/H+ exchanger inhibitor, and its inhibition of iNOS induction in hepatic ischemia-reperfusion injury in rats. Shock. 2008 Sep;30(3):311-7.

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