YM-244769 hydrochloride

Cat. No.: HY-107659

CAS No.: 837424-39-2

Molecular Formula: $C_{26}H_{23}ClFN_3O_3$

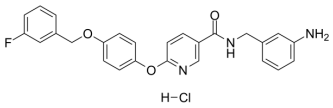
Molecular Weight: 479.93

Target: Na+/Ca2+ Exchanger

Pathway: Membrane Transporter/Ion Channel

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 (208.36 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0836 mL	10.4182 mL	20.8364 mL
	5 mM	0.4167 mL	2.0836 mL	4.1673 mL
	10 mM	0.2084 mL	1.0418 mL	2.0836 mL

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

BIOLOGICAL ACTIVITY

Description

YM-244769 hydrochloride is a potent, selective and orally active Na^+/Ca^{2+} exchanger (NCX) inhibitor. YM-244769 hydrochloride preferentially inhibits NCX3 and suppresses the unidirectional outward NCX current (Ca^{2+} entry mode), with IC_{50}s of 18 nM and 50 nM, respectively. YM-244769 hydrochloride efficiently protects against hypoxia/reoxygenation-induced SH-SY5Y neuronal cell damage. YM-244769 hydrochloride can also increase urine volume and urinary excretion of electrolytes in mice[1][2][3].

IC_{50} & Target

IC_{50}: 18 nM (NCX3)[1]

In Vitro

YM-244769 (0.003-1 μM) inhibits dose dependently the initial rates of $^{45}Ca^{2+}$ uptake into NCX1, NCX2, and NCX3 transfectants with IC_{50} values of 68 ± 2.9, 96 ± 3.5, and 18 ± 1.0 nM, respectively[1].

YM-244769 (0.3 or 1 μM) efficiently protects against the hypoxia/reoxygenation-induced lactate dehydrogenase (LDH) release in SH-SY5Y cells and in LLC-PK_1 cells (1 μM)[1].

YM-244769 possesses reverse mode-selectivity[1].

YM-244769 (1 and 10 μM) inhibits NCX current (I_{NCX}) in a concentration- and $[Na^+]_i$-dependent manner, the IC_{50} against the unidirectional outward I_{NCX} (Ca^{2+} entry mode) is 0.05 μM. The IC_{50} values against the bidirectional outward and inward I_{NCX}

	are similar and approximately 100 nM with a Hill coefficient of about 1[3]. YM-244769 is trypsin-insensitive[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	YM-244769 (0.1-1 mg/kg; p.o.; once) exhibits dose-dependently natriuretic action in mice and significantly increased urinary excretion of Ca^{2+} as well as Ca^{2+}/Cr ratio[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Wild-type C57BL/6J mice and NCX-KO mice[2]
Dosage:	0.1, 0.3 and 1 mg/kg
Administration:	Oral administration, once
Result:	Caused a dose-dependent increase (up to approximately 200%) in urine volume and urinary excretion of electrolytes (Na^+, K^+ and Cl^-). Natriuretic actions were equivalently observed in NCX1-KO and WT, but disappeared in NCX2-KO and double KO.

REFERENCES

[1]. Iwamoto T, Kita S. YM-244769, a novel Na+/Ca2+ exchange inhibitor that preferentially inhibits NCX3, efficiently protects against hypoxia/reoxygenation-induced SH-SY5Y neuronal cell damage. Mol Pharmacol. 2006 Dec;70(6):2075-83.

[2]. Gotoh Y, et al. Genetic knockout and pharmacologic inhibition of NCX2 cause natriuresis and hypercalciuria. Biochem Biophys Res Commun. 2015 Jan 9;456(2):670-5.

[3]. Yamashita K, et al. Inhibitory effect of YM-244769, a novel Na+/Ca2+ exchanger inhibitor on Na+/Ca2+ exchange current in guinea pig cardiac ventricular myocytes. Naunyn Schmiedebergs Arch Pharmacol. 2016 Nov;389(11):1205-1214.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA