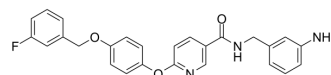


YM-244769

Cat. No.:	HY-136182A
CAS No.:	838819-70-8
Molecular Formula:	C ₂₆ H ₂₂ FN ₃ O ₃
Molecular Weight:	443.47
Target:	Na ⁺ /Ca ²⁺ Exchanger
Pathway:	Membrane Transporter/Ion Channel
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro	DMSO : 120 mg/mL (270.59 mM; Need ultrasonic)						
	Preparing Stock Solutions	Solvent Concentration	Mass	1 mg	5 mg	10 mg	
				1 mM	2.2549 mL	11.2747 mL	22.5494 mL
				5 mM	0.4510 mL	2.2549 mL	4.5099 mL
				10 mM	0.2255 mL	1.1275 mL	2.2549 mL
Please refer to the solubility information to select the appropriate solvent.							
In Vivo	1. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.08 mg/mL (4.69 mM); Clear solution						

BIOLOGICAL ACTIVITY

Description	YM-244769 is a potent, selective and orally active Na ⁺ /Ca ²⁺ exchanger (NCX) inhibitor. YM-244769 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 efficiently protects against hypoxia/reoxygenation-induced SH-SY5Y neuronal cell damage. YM-244769 can also increase urine volume and urinary excretion of electrolytes in mice ^{[1][2][3]} .
IC ₅₀ & Target	IC ₅₀ : 18 nM (NCX3), 68 nM (NCX1), 96 nM (NCX2) ^[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.

Cell Viability Assay^[1]

Cell Line:	SH-SY5Y cells treated with NCX1 or NCX3 antisense
Concentration:	0.3 and 1 μ M
Incubation Time:	
Result:	Hypoxia/reoxygenation-induced LDH release was significantly attenuated: reduction in cell damage was greater in cells treated with NCX3 antisense (by 61%) than in cells treated with NCX1 antisense (by 35%). 0.3 or 1 μ M efficiently suppressed the hypoxia/reoxygenation-induced cell damage in SH-SY5Y cells treated with NCX1 antisense more than in those treated with NCX3 antisense.

In Vivo

YM-244769 (0.1-1 mg/kg; p.o.; once) exhibits dose-dependently natriuretic action in mice and significantly increases 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 $\text{Na}^+/\text{Ca}^{2+}$ 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 $\text{Na}^+/\text{Ca}^{2+}$ exchanger inhibitor on $\text{Na}^+/\text{Ca}^{2+}$ exchange current in guinea pig cardiac ventricular myocytes. *Naunyn Schmiedebergs Arch Pharmacol*. 2016 Nov;389(11):1205-1214.

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

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