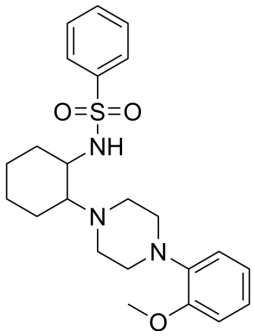
ML-SI3

Cat. No.:	HY-139426
CAS No.:	891016-02-7
Molecular Formula:	$C_{23}H_{31}N_3O_3S$
Molecular Weight:	430
Target:	TRP Channel; Parasite
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling; Anti-infection
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 : 50 mg/mL (116.28 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3256 mL	11.6279 mL	23.2558 mL
	5 mM	0.4651 mL	2.3256 mL	4.6512 mL
	10 mM	0.2326 mL	1.1628 mL	2.3256 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: ≥ 2.5 mg/mL (5.81 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ML-SI3 is a mixture of cis/trans ML-SI3. ML-SI3 is a TRPML channel modulator. ML-SI3 blocks TRPML1 and TRPML2 with IC_{50}s of 4.7 μM and 1.7 μM, respectively. ML-SI3 is also able to activate TRPML2 and TRPML3 with EC_{50}s of 3.3-9.4 μM and 29 μM, respectively. ML-SI3 also inhibits lysosomal calcium efflux and blocks downstream TRPML1-mediated autophagy.

IC_{50} & Target	Schistosome	TRPML1	TRPML2	TRPML3
		4.7 μM (IC_{50})	1.7 μM (IC_{50})	12.5 μM (IC_{50})

In Vitro

ML-SI3 (10 μM) inhibits ML-SA1-evoked Ca^{2+} signals in HeLa cells[2].
ML-SI3 (25-75 μM, 24h) disrupts tegumental integrity of adult schistosomes[3].
ML-SI3 (10 μM) blocks Rapamycin (HY-10219)-evoked I_{TRPML1} in mimic of lysosomal lumen[4].
ML-SI3 (3 μM, 6 h) abolishes the increase in both LC3II and p62 levels induced by hypoxia/reoxygenation (H/R) (4 h H/2 h R) in neonatal rat ventricular myocytes (NRVM)[5].

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

In Vivo

ML-SI3 (1.5 mg/kg, i.p., four times) attenuates I/R injury in mouse cardiomyocytes[5].

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Animal Model:	Myocardial Ischemia/reperfusion (I/R) injury mice[5]
Dosage:	1.5 mg/kg
Administration:	Intraperitoneal injection (i.p.), four times before and during the in vivo I/R (ischemia 30 min and reperfusion 1 day)
Result:	Restored the blocked autophagic fux in the cardiomyocytes subjected to I/R.

REFERENCES

[1]. Rühl P, et al. Estradiol analogs attenuate autophagy, cell migration and invasion by direct and selective inhibition of TRPML1, independent of estrogen receptors. Sci Rep. 2021 Apr 15;11(1):8313.

[2]. Kilpatrick BS, et al. Endo-lysosomal TRP mucolipin-1 channels trigger global ER Ca2+ release and Ca2+ influx. J Cell Sci. 2016 Oct 15;129(20):3859-3867.

[3]. Bais S, et al. Schistosome TRPML channels play a role in neuromuscular activity and tegumental integrity. Biochimie. 2022 Mar;194:108-117.

[4]. Zhang X, et al. Rapamycin directly activates lysosomal mucolipin TRP channels independent of mTOR. PLoS Biol. 2019 May 21;17(5):e3000252.

[5]. Xing Y, et al. Blunting TRPML1 channels protects myocardial ischemia/reperfusion injury by restoring impaired cardiomyocyte autophagy. Basic Res Cardiol. 2022 Apr 7;117(1):20.

[6]. Leser C, et al. Chemical and pharmacological characterization of the TRPML calcium channel blockers ML-SI1 and ML-SI3. Eur J Med Chem. 2021 Jan 15;210:112966.

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