KB-R7943 mesylate

Cat. No.: HY-15415

CAS No.: 182004-65-5

Molecular Formula: $C_{17}H_{21}N_3O_6S_2$

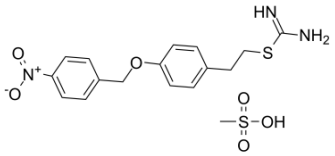
Molecular Weight: 427.5

Target: Na+/Ca2+ Exchanger; Autophagy

Pathway: Membrane Transporter/Ion Channel; Autophagy

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 : ≥ 27 mg/mL (63.16 mM)

H_2O : 4.3 mg/mL (10.06 mM; Need warming)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Mass / Solvent / Concentration	1 mg	5 mg	10 mg
1 mM	2.3392 mL	11.6959 mL	23.3918 mL
5 mM	0.4678 mL	2.3392 mL	4.6784 mL
10 mM	0.2339 mL	1.1696 mL	2.3392 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.85 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.85 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.85 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

KB-R7943 mesylate is a widely used inhibitor of the reverse Na^+/Ca^{2+} exchanger (NCX_{rev}) with IC_{50} of 5.7±2.1 μM. KB-R7943 mesylate induces cancer cell death via activating the JNK pathway and blocking autophagic flux.

IC_{50} & Target

IC50: 5.7±2.1 μM (Na^+/Ca^{2+} exchanger)[1]

In Vitro

KB-R7943 mesylate blocks NMDAR-mediated ion currents, and inhibits NMDA-induced increase in cytosolic Ca^{2+} with IC_{50} =13.4±3.6 μM but accelerates calcium deregulation and mitochondrial depolarization in glutamate-treated neurons. KB-R7943 depolarizes mitochondria in a Ca^{2+}-independent manner. KB-R7943 inhibits 2,4-dinitrophenol-stimulated respiration of cultured neurons with IC_{50}=11.4±2.4 μM. In addition to NCX_{rev}, KB-R7943 dose-dependently and reversibly blocked ion currents elicited by NMDA. KB-R7943 dose-dependently inhibits NMDA-induced increases in $[Ca^{2+}]_c$ with IC_{50}=13.4±3.6 μM confirming the inhibition of NMDA receptors observed in electrophysiological experiments[1]. $_{wt}$RyR1-HEK 293 pretreated with KB-R7943 (10 μM, 10 min) dissolved in the bulk perfusion exhibited significantly attenuated responses to caffeine. In this regard, KB-R7943 produced more pronounced inhibition of caffeine-induced Ca^{2+} release elicited by 1 mM compared with 0.5 and 0.75 mM (60 versus 58 versus 37%, $p<0.05$, respectively)[2]. KB-R7943 inhibits both I_{hERG} and native I_{Kr} rapidly on membrane depolarization with IC_{50} values of ~89 and ~120 nM, respectively, for current tails at −40 mV following depolarizing voltage commands to +20 mV. I_{hERG} inhibition by KB-R7943 exhibits both time- and voltage-dependence but shows no preference for inactivated over activated channels[3].

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

PROTOCOL

Cell Assay [2]

EK 293 cells stably expressing the $_{wt}$RyR1 ($_{wt}$RyR1-HEK 293) are maintained in Dulbecco's modified Eagle's medium supplemented with 2 mM glutamine, 100 μg/mL streptomycin, 100 U/mL penicillin, 1 mM sodium pyruvate, and 10% fetal bovine serum at 37°C under 5% CO_2. $_{wt}$RyR1-HEK 293 cells are loaded with 5 μM Fluo-4 acetoxymethyl ester at 37°C for 30 min to measure Ca^{2+} transients in an imaging buffer consisting of 140 mM NaCl, 5 mM KCl, 2 mM $MgCl_2$, 2 mM $CaCl_2$, 10 mM HEPES, and 10 mM glucose, pH 7.4, supplemented with 0.05% bovine serum albumin. The cells are washed three times with imaging buffer and additionally incubated for 20 min at room temperature. Dye-loaded cells are washed three times with imaging buffer and imaged with a charge-coupled device camera with a 40× objective lens attached to an IX-71 microscope. The sequence of images is captured and monitored using EasyRatioPro. Caffeine dissolved in the imaging buffer is focally applied for 15 s using AutoMate Scientific. KB-R7943 is dissolved in the imaging buffer, and $_{wt}$RyR1-HEK 293 cells are incubated for 10 min before the application of caffeine[2].

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

REFERENCES

[1]. Brustovetsky T, et al. KB-R7943, an inhibitor of the reverse Na+ /Ca2+ exchanger, blocks N-methyl-D-aspartate receptor and inhibits mitochondrial complex I. Br J Pharmacol. 2011 Jan;162(1):255-70.

[2]. Barrientos G, et al. The Na+/Ca2+ exchange inhibitor 2-(2-(4-(4-nitrobenzyloxy)phenyl)ethyl)isothiourea methanesulfonate(KB-R7943) also blocks ryanodine receptors type 1 (RyR1) and type 2 (RyR2) channels. Mol Pharmacol. 2009 Sep;76(3):560-8.

[3]. Cheng H, et al. High potency inhibition of hERG potassium channels by the sodium-calcium exchange inhibitor KB-R7943. Br J Pharmacol. 2012 Apr;165(7):2260-73.

[4]. Long Z, et al. The reverse-mode NCX1 activity inhibitor KB-R7943 promotes prostate cancer cell death by activating the JNK pathway and blocking autophagic flux. Oncotarget. 2016;7(27):42059-70.

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