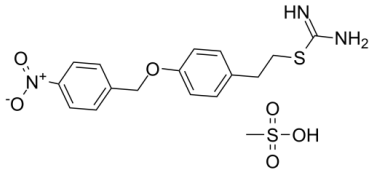
Data Sheet

Product Name:	KB-R7943 (mesylate)
Cat. No.:	CS-0848
CAS No.:	182004-65-5
Molecular Formula:	C17H21N3O6S2
Molecular Weight:	427.50
Target:	Autophagy; Na+/Ca2+ Exchanger
Pathway:	Autophagy; Membrane Transporter/Ion Channel
Solubility:	DMSO : ≥ 27 mg/mL (63.16 mM); H2O : 4.3 mg/mL (10.06 mM; Need warming)



BIOLOGICAL ACTIVITY:

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. IC50 & 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].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: KB-R7943 mesylate is dissolved in DMSO and stored, and then diluted with appropriate medium before use[2].[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].

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.

CAIndexNames:

Carbamimidothioic acid, 2-[4-[(4-nitrophenyl)methoxy]phenyl]ethyl ester, methanesulfonate (1:1)

SMILES:

NC(SCCC1=CC=C(OCC2=CC=C([N+]([O-])=O)C=C2)C=C1)=N.CS(=O)(O)=O

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