# 产品名称：2-[2-[4-(4-Nitrobenzyloxy)Phenyl]Ethyl]Isothiourea Mesylate
# 产品别名：KB-R7943 mesylate

## 生物活性：

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| **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]. |
| **Solvent&Solubility** | ***In Vitro:***<br>**DMSO : ≥ 27 mg/mL (63.16 mM)**<br>**$H_2O$ : 4.3 mg/mL (10.06 mM;** Need warming)<br>* "≥" means soluble, but saturation unknown. |

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
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| 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 |

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

***In Vivo:***

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (5.85 mM); Clear solution

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| | 此方案可获得 ≥ 2.5 mg/mL (5.85 mM，饱和度未知) 的澄清溶液。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL<br><br>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)<br>Solubility: ≥ 2.5 mg/mL (5.85 mM); Clear solution<br>此方案可获得 ≥ 2.5 mg/mL (5.85 mM，饱和度未知) 的澄清溶液。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。<br><br>3.请依序添加每种溶剂： 10% DMSO →90% corn oil<br>Solubility: ≥ 2.5 mg/mL (5.85 mM); Clear solution<br>此方案可获得 ≥ 2.5 mg/mL (5.85 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。 |
| **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.<br>[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.<br>[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.<br>[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. |

**实验参考：**

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| **Cell Assay** | 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]. |
| | [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.<br>[2]. Barrientos G, et al. The Na+/Ca2+ exchange inhibitor |

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