KB-R7943 mesylate

Cat. No.: HY-15415
CAS No.: 182004-65-5
Molecular Formula: C₁₇H₂₁N₃O₆S₂
Molecular Weight: 427.5
Target: Na+/Ca2+ Exchanger
Pathway: Membrane Transporter/Ion Channel
Storage:
- Powder: -20°C 3 years
- 4°C: 2 years
- In solvent:
  - -80°C: 6 months
  - -20°C: 1 month

**SOLVENT & SOLUBILITY**

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMSO</td>
<td>≥ 27 mg/mL (63.16 mM)</td>
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<tr>
<td>H₂O</td>
<td>4.3 mg/mL (10.06 mM; Need warming)</td>
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</tbody>
</table>

* “≥” means soluble, but saturation unknown.

**Preparing Stock Solutions**

- 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.

**BIOLOGICAL ACTIVITY**

**Description**

KB-R7943 mesylate is a widely used inhibitor of the reverse Na⁺/Ca²⁺ exchanger (NCXₜᵣᵥ) with IC₅₀ of 5.7±2.1 µM.

**IC₅₀ & Target**

IC₅₀: 5.7±2.1 µM (Na⁺/Ca²⁺ exchanger) [¹]

**In Vitro**

KB-R7943 mesylate blocks NMDAR-mediated ion currents, and inhibits NMDA-induced increase in cytosolic Ca²⁺ with IC₅₀=13.4±3.6 µM but accelerates calcium deregulation and mitochondrial depolarization in glutamate-treated neurons. KB-R7943 depolarizes mitochondria in a Ca²⁺-independent manner. KB-R7943 inhibits 2,4-dinitrophenol-stimulated respiration of cultured neurons with IC₅₀=11.4±2.4 µM. In addition to NCXₜᵣᵥ, KB-R7943 dose-dependently and reversibly blocked ion currents elicited by NMDA. KB-R7943 dose-dependently inhibits NMDA-induced increases in [Ca²⁺]c with IC₅₀=13.4±3.6 µM confirming the inhibition of NMDA receptors observed in electrophysiological experiments [²]. wTÀR1-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\textsuperscript{2+} release elicited by 1 mM compared with 0.5 and 0.75 mM (60 versus 58 versus 37\%, p<0.05, respectively)\textsuperscript{[2]}. KB-R7943 inhibits both \textsubscript{i}hERG and native \textsubscript{i}K\textsubscript{r} rapidly on membrane depolarization with \textit{IC}_{50} values of \textasciitilde 89 and \textasciitilde 120 nM, respectively, for current tails at \textasciitilde 40 mV following depolarizing voltage commands to +20 mV. \textsubscript{i}hERG inhibition by KB-R7943 exhibits both time- and voltage-dependence but shows no preference for inactivated over activated channels\textsuperscript{[3]}.

**PROTOCOL**

**Cell Assay** \textsuperscript{[2]}

EK 293 cells stably expressing the \textsubscript{wt}RyR1 (\textsubscript{wt}RyR1-HEK 293) are maintained in Dulbecco’s modified Eagle’s medium supplemented with 2 mM glutamine, 100 \textmu g/mL streptomycin, 100 U/mL penicillin, 1 mM sodium pyruvate, and 10% fetal bovine serum at 37\Celsius under 5% CO\textsubscript{2}. \textsubscript{wt}RyR1-HEK 293 cells are loaded with 5 \mu M Fluo-4 acetoxymethyl ester at 37\Celsius for 30 min to measure Ca\textsuperscript{2+} transients in an imaging buffer consisting of 140 mM NaCl, 5 mM KCl, 2 mM MgCl\textsubscript{2}, 2 mM CaCl\textsubscript{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\times 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 \textsubscript{wt}RyR1-HEK 293 cells are incubated for 10 min before the application of caffeine\textsuperscript{[2]}. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**REFERENCES**


[2]. Barrientos G, et al. The Na\textsuperscript{+}/Ca\textsuperscript{2+} 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.