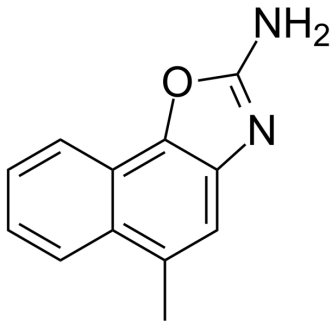
SKA-121



Cat. No.:	HY-107414
CAS No.:	1820708-73-3
Molecular Formula:	$C_{12}H_{10}N_2O$
Molecular Weight:	198.22
Target:	Potassium Channel
Pathway:	Membrane Transporter/Ion Channel
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year

SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 42.86 mg/mL (216.22 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	5.0449 mL	25.2245 mL	50.4490 mL
	5 mM	1.0090 mL	5.0449 mL	10.0898 mL
	10 mM	0.5045 mL	2.5224 mL	5.0449 mL

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

BIOLOGICAL ACTIVITY

Description

SKA-121 is a selective $K_{Ca}3.1$ activator. SKA-121 exhibits EC_{50}s of 109 nM and 4.4 μM for $K_{Ca}3.1$ and $K_{Ca}2.3$, respectively.

IC_{50} & Target

EC50: 109 nM ($K_{Ca}3.1$), 4.4 μM ($K_{Ca}2.3$)[1]

In Vitro

SKA-121, a compound generated through an isosteric replacement approach. SKA-121 is a typical positive-gating modulator and shifts the calcium-concentration response curve of $K_{Ca}3.1$ to the left. SKA-121 displays 41-fold selectivity for $K_{Ca}3.1$ (EC_{50} 109 nM±14 nM) over $K_{Ca}2.3$ (EC_{50} 4.4 ± 1.6 μM). SKA-121 is 200- to 400-fold selective over representative K_V ($K_V1.3$, $K_V2.1$, $K_V3.1$, and $K_V11.1$), Na_V ($Na_V1.2$, $Na_V1.4$, $Na_V1.5$, and NaV1.7), as well as $Ca_V1.2$ channels[1].

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

In Vivo

In blood pressure telemetry experiments, SKA-121 (100 mg/kg i.p.) significantly lowers mean arterial blood pressure in normotensive and hypertensive wild-type but not in $K_{Ca}3.1^{-/-}$ mice. SKA-121 can be used as a new $K_{Ca}3.1$ selective pharmacological tool compound despite its relatively short half-life in mice. A lower dose of 30 mg/kg of SKA-121 does not produce significant alterations in MAP. The vehicle, peanut oil/DMSO (9:1 v/v, for SKA-121), does not cause significant

	alterations in MAP or HR. SKA-121 has a short half-life (~20 minutes), and plasma decay is extremely rapid (21.3±2.4 μM at 5 minutes; 483±231 nM at 1 hour and 53±44 nM at 4 hours). Since SKA-121 is relatively well soluble (logP=1.79) and can potentially be added to drinking water in animal experiments, it orally is also administered, and find that it has an oral availability of roughly 25%[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	To fully evaluate the selectivity of the naphthooxazole SKA-121, seven-point concentration-response curves on $K_{Ca}2.1$, $K_{Ca}2.2$, $K_{Ca}2.3$ and $K_{Ca}3.1$ are determined with 250 nM free Ca^{2+} in the internal solution[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Twelve-week-old male C57Bl/6J mice are used. For i.v. application, SKA-121 is dissolved at 5 mg/mL in a mixture of 10% CremophorEL and 90% phosphate-buffered saline and then injected at 10 mg/kg into the tail vein (n=8 mice per compound). Another group of mice (n=8) receive SKA-121 orally. At various time points after the injection, blood is collected into EDTA blood sample collection tubes either from the saphenous vein or by cardiac puncture under deep isoflurane anesthesia. After the cardiac puncture, mice are sacrificed by cutting the heart, and then the brain is removed. Individual mice are typically used for three times points (two blood collections from the saphenous vein plus the terminal blood collection). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Int J Mol Sci. 2022 Aug 3;23(15):8603.

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REFERENCES

[1]. Coleman N, et al. New positive Ca2+-activated K+ channel gating modulators with selectivity for KCa3.1. Mol Pharmacol. 2014 Sep;86(3):342-57.

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