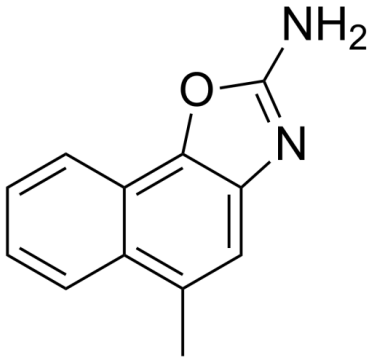
Data Sheet

Product Name:	SKA-121
Cat. No.:	CS-7918
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
Solubility:	DMSO : ≥ 42.86 mg/mL



BIOLOGICAL ACTIVITY:

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. IC50 & 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]. ***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].

PROTOCOL (Extracted from published papers and Only for reference)

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].

Animal Administration: SKA-121 is dissolved at 5 mg/mL in a mixture of 10% CremophorEL and 90% phosphate-buffered saline (Mice)[1].[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).

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.

CAIndexNames:

Naphth[2,1-d]oxazol-2-amine, 5-methyl-

SMILES:

NC1=NC2=CC(C)=C3C=CC=CC3=C2O1

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