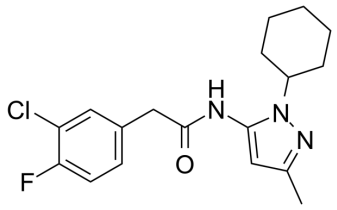
VU0810464

Cat. No.:	HY-127106
CAS No.:	2126040-21-7
Molecular Formula:	$C_{18}H_{21}ClFN_3O$
Molecular Weight:	349.83
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 : ≥ 250 mg/mL (714.63 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.8585 mL	14.2927 mL	28.5853 mL
5 mM	0.5717 mL	2.8585 mL	5.7171 mL
10 mM	0.2859 mL	1.4293 mL	2.8585 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (5.95 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

VU0810464 is a potent and selective non-ureaG protein-gated inwardly-rectifying potassium channels (GIRK, Kir3) activator. VU0810464 displays nanomolar potency for neuronal (EC_{50}=165 nM) and GIRK1/4 (EC_{50}=720 nM) channels with improved brain penetration[1][2].

IC_{50} & Target

EC50: 165 nM (GIRK 1/2); 720 nM (GIRK1/4)[1][2]

In Vitro

VU0810464 (0, 0.1, 0.3, 1, 3, 10, 30 μM) produces a concentration⊠dependent response curves of currents in SAN and HPC cells, in addition, VU0810464 is 9⊠fold higher potency for Kir3 channel activation in neurons as compared to SAN cells[2].

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

In Vivo

VU0810464 (intraperitoneal injection; 30 mg/kg, 10 mg/kg; 30mg/kg; pre-treated 30 mins) produces a dose-dependent

reduction of SIH response in Male C57BL/6J mice. To test if VU0810464 plays it role through Kir3 channel activation, VU0810464 (10 mg/kg) suppresses the SIH response in wild‐type mice, but has no impact on Kcnj3$^{-/-}$ mice[2]. VU0810464 (intraperitoneal injection ; 30 mg/kg; 15, 30, 45, or 60 min post‐injection) displays a favourable distribution to the brain ($K_{p,uu}$ = 0.83), has a improvement over ML297 ($K_{p,uu}$= 0.32). Clearance of VU0810464 is rapid,brain and plasma half-lives is 20 min in a PK study[2].

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Animal Model:	Male C57BL/6J mice, Kcnj3$^{-/-}$ siblings female and male C57BL/6J mice
Dosage:	10 mg/kg; 30mg/kg
Administration:	Intraperitoneal injection
Result:	Reduced stress‐induced hyperthermia (SIH), a physiological test ofanxiolytic efficacy in wild mice, but had no impact in and Kcnj3 (Girk1) $^{-/-}$ mice.

REFERENCES

[1]. Vo BN, et al. VU0810464, a non-urea G protein-gated inwardly rectifying K+ (Kir 3/GIRK) channel activator, exhibits enhanced selectivity for neuronal Kir 3 channels and reduces stress-induced hyperthermia in mice.Br J Pharmacol. 2019 Jul;176(13):2238-2249

[2]. Wieting JM,et al. Discovery and Characterization of 1H-Pyrazol-5-yl-2-phenylacetamides as Novel, Non-Urea-Containing GIRK1/2 Potassium Channel Activators.ACS Chem Neurosci. 2017 Sep 20;8(9):1873-1879.

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