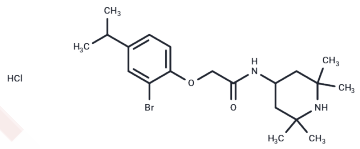
Data Sheet (Cat.No.T13316)

TargetMol

VU0134992 hydrochloride

Chemical Properties



CAS No. : 1052515-91-9

Formula: C20H32BrClN2O2

Molecular Weight: 447.84

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	VU0134992 hydrochloride is the first subtype-preferring, orally active and selective blocker of the Kir4.1 potassium channel pore (IC50: 0.97 μM).
Targets(IC50)	Potassium Channel
In vitro	In whole-cell patch-clamp electrophysiology experiments, VU0134992 inhibits Kir4.1 with an IC50 value of 0.97 M and is 9-fold selective for homomeric Kir4.1 over Kir4.1/5.1 concatemeric channels (IC50 = 9 M) at -120 mV. In thallium (Tl+) flux assays, VU0134992 is greater than 30-fold selective for Kir4.1 over Kir1.1, Kir2.1, and Kir2.2; is weakly active toward Kir2.3, Kir6.2/SUR1, and Kir7.1; and is equally active toward Kir3.1/3.2, Kir3.1/3.4, and Kir4.2. This potency and selectivity profile is superior to Kir4.1 inhibitors amitriptyline, nortriptyline, and fluoxetine. Medicinal chemistry identified components of VU0134992 that are critical for inhibiting Kir4.1. Patch-clamp electrophysiology, molecular modeling, and site-directed mutagenesis identified pore-lining glutamate 158 and isoleucine 159 as critical residues for block of the channel.
In vivo	VU0134992 displayed a large free unbound fraction (fu) in rat plasma (fu = 0.213). Consistent with the known role of Kir4.1 in renal function, oral dosing of VU0134992 led to a dose-dependent diuresis, natriuresis, and kaliuresis in rats.Thus, VU0134992 represents the first in vivo active tool compound for probing the therapeutic potential of Kir4.1 as a novel diuretic target for the treatment of hypertension.
Animal Research	VU0134992 hydrochloride (250-300 g Male Sprague-Dawley rats;50 and 100 mg/kg) Oral gavage

Solubility Information

Solubility	DMSO: 230 mg/mL (513.58 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 5 mg/mL (11.16 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2329 mL	11.1647 mL	22.3294 mL
5 mM	0.4466 mL	2.2329 mL	4.4659 mL
10 mM	0.2233 mL	1.1165 mL	2.2329 mL
50 mM	0.0447 mL	0.2233 mL	0.4466 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Kharade SV, et al. Discovery, Characterization, and Effects on Renal Fluid and Electrolyte Excretion of the Kir4.1 Potassium Channel Pore Blocker, VU0134992. Mol Pharmacol. 2018 Aug;94(2):926-937.