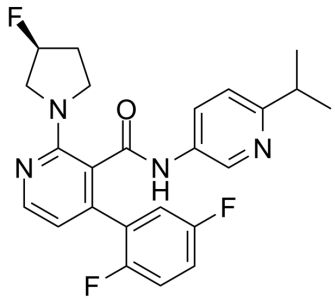
Nav1.1 activator 1

Cat. No.:	HY-126429
CAS No.:	2332897-85-3
Molecular Formula:	$C_{24}H_{23}F_3N_4O$
Molecular Weight:	440.46
Target:	Sodium 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 (567.59 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2704 mL	11.3518 mL	22.7035 mL
	5 mM	0.4541 mL	2.2704 mL	4.5407 mL
	10 mM	0.2270 mL	1.1352 mL	2.2704 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 (4.72 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.72 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.72 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Nav1.1 activator 1 (compound 4), a highly potent $Na_V1.1$ activator with BBB penetration, increases decay time constant (tau) of $Na_V1.1$ currents at 0.03 μM along with significant selectivity against $Na_V1.2$, $Na_V1.5$, and $Na_V1.6$[1].

IC_{50} & Target

$Na_V1.1$[1].

In Vivo

Nav1.1 activator 1 (compound 4) is a valuable $Na_V1.1$ activator for further evaluation of pathophysiological functions of the Nav1.1 channel and has potential for therapeutic treatments of CNS diseases such as Dravet syndrome[1].

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

Animal Model:	Mice[1].
Dosage:	30 mg/kg (Pharmacokinetic Analysis).
Administration:	IP once (Exposure was measured at 1 h after administration).
Result:	Intraperitoneal administration (30 mg/kg) of compound resulted in sufficient brain exposure (193 ng/g 1 h after administration), which corresponded to 13 nM of free brain concentration comparable to the in vitro potency of the compound. Had a potential use as an in vivo tool to investigate whether this type of $Na_v1.1$ activator can restore $Na_v1.1$ functions and modify the disease state in animal models. Could penetrate the blood-brain barrier (BBB) in humans.

REFERENCES

[1]. Miyazaki T, et al. Discovery of novel 4-phenyl-2-(pyrrolidinyl)nicotinamide derivatives as potent Nav1.1 activators. Bioorg Med Chem Lett. 2019 Mar 15;29(6):815-820.

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