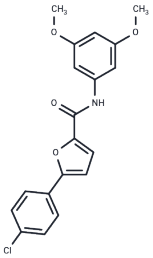
Data Sheet (Cat.No.T2024)

TargetMol

A-803467

Chemical Properties



CAS No. : 944261-79-4

Formula: C19H16ClNO4

Molecular Weight: 357.79

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	A-803467 is a selective NaV1.8 channel blocker.
Targets(IC50)	Sodium Channel
In vitro	A-803467 effectively reduced pain sensitivity in a dose-dependent manner in models including spinal nerve ligation (ED50 = 47 mg/kg, ip), sciatic nerve injury (ED50 = 85 mg/kg, ip), capsaicin-induced secondary mechanical allodynia (ED50 ≈ 100 mg/kg, intraperitoneally), and hyperalgesia following complete Freund's adjuvant injection into the plantar foot (ED50 = 41 mg/kg, intraperitoneally). Consistent with its effects on neuronal action potentials in vitro, systemic administration of A-803467 (20 mg/kg, iv) to rats with spinal nerve ligation significantly reduced both spontaneous and von Frey hair-induced responses in wide dynamic range neurons of the spinal cord dorsal horn by 66% and 53%, respectively. However, A-803467 was ineffective in models of harm induced by formalin, as well as acute thermal, postoperative pain, and pain caused by chemotherapy (vincristine).
In vivo	A-803467 selectively blocks tetrodotoxin-resistant (TTX-R) currents in rat dorsal root ganglion neurons in a concentration-dependent manner, with an IC50 of 140 nM, proving more effective than mexiletine and lamotrigine (IC50> 30 μM). It exhibits 300 to 1,000 times higher selectivity for hNaV1.8 over hNaV1.2, hNaV1.3, hNaV1.5, and hNaV1.7 channels, with respective IC50 values of 7.38 μM, 2.45 μM, 7.34 μM, and 6.74 μM. A-803467 shows no significant activity against other channels and receptors expressed in peripheral sensory neurons (including TRPV1, P2X2/3, CaV2.2, and KCNQ2/3 channels), with an IC50 > 10 μM. It effectively blocks recombinant human or rat Nav1.8 channels at IC50s of 8 nM and 45 nM, maintained at a -40 mV potential. A-803467 also blocks human NaV1.8 channels in a resting state, with an IC50 of 79 nM.
Kinase Assay	Maize HD2, HD1-B, and HD1-A Enzyme Inhibition.: The enzyme liberats tritiated acetic acid from the substrate, which is quantified by scintillation counting. IC50 values are results of triple determinations. A 50 μL sample of maize enzyme (at 30 °C) is incubated (30 min) with 10 μL of total [3H]acetate-prelabeled chicken reticulocyte histones (2 mg/mL). Reaction is stopped by addition of 50 μL of 1 M HCl/0.4 M acetate and 800 μL of ethyl acetate. After centrifugation (1×104 g, 5 min), an aliquot of 600 μL of the upper phase is counted for radioactivity in 3 mL of liquid scintillation cocktail. MC1568 is tested at a starting concentration of 40 μM, and active substances are diluted further. NaB,

Kinase Assay	VPA, TSA, SAHA, 85 TPX, HC-toxin, and tubacin are used as the reference compounds, and blank solvents are used as negative controls.

Solubility Information

Solubility	Ethanol: 8.9 mg/mL (24.87 mM),Sonication is recommended. DMSO: 65 mg/mL (181.67 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: 2 mg/mL (5.59 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	2.7949 mL	13.9747 mL	27.9494 mL
5 mM	0.559 mL	2.7949 mL	5.5899 mL
10 mM	0.2795 mL	1.3975 mL	2.7949 mL
50 mM	0.0559 mL	0.2795 mL	0.559 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

Jarvis MF, et al. Proc Natl Acad Sci U S A, 2007, 104(20), 8520-8525.
Qi B, Dai S, Song Y, et al. Blockade of NaV1.8 Increases the Susceptibility to Ventricular Arrhythmias During Acute Myocardial Infarction. Frontiers in Cardiovascular Medicine. 2021, 8
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Joshi SK, et al. J Pain, 2009, 10(3), 306-315.
Dai S P, Yang C C, Chin Y, et al.TDAG8-mediated distinct signaling pathways modulate the early and late phases of neuropathic pain.iScience.2024
Qi B, Xie Z, Shen D, et al.Blocking NaV1. 8 regulates atrial fibrillation inducibility and cardiac conduction after myocardial infarction.BMC Cardiovascular Disorders.2024, 24: 605.