Product Data Sheet

Product Name: A 887826
Cat. No.: GC14481

Chemical Properties

Cas. No.	1266212-81-0		
Chemical Name	5-(4-butoxy-3-chlorophenyl)-N-((2-morpholinopyridin-3-yl)methyl)nicotinamide		
SMILES	ClC1=CC(C2=CN=CC(C(NCC3=CC=CN=C3N4CCOCC4)=O)=C2)=CC=C1OCCCC		
Formula	$C_{26}H_{29}ClN_4O_3$	M.Wt	480.99
Solubility	<24.05mg/ml in DMSO	Storage	Store at RT
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	A 887826		

Background

A 887826 is a potent and voltage-dependent Nav1.8 sodium channel blocker. It blocked recombinant human Nav1.8 channels with an IC50 value of 11nM [1].

Voltage-gated sodium channels are important in the generation and propagation of action potential. At least 9 genes encode functional sodium channels, namely Nav1.1-Nav1.9. Nav1.8 is a TTX-resistant (TTX-R) sodium channel. Nav1.8 is highly localized on primary sensory afferent neurons. Nav1.8 is involved in the processing of nociceptive information.

-100 mV without prepulse did make a resting state for rat DRG neurons. Prepulse to -40 mV did make an inactivated state for channels. In rat DRG neurons in these two states, treatment with A 887826 at 1 μM significantly blocked TTXR Na+ currents. A 887826 blocked TTX-R Na+ currents with an IC50 value of 7.9 ± 0.2 nM (n= 5~9) when channels were in an inactivated state (-40 mV). A 887826 showed an IC50 value of 63.6 ± 0.2 nM (n=5~9) to less depolarized (at -60, -80 or -100 mV) TTX-R Na+ currents. That meant A 887826 state-dependently blocked TTX-R Na+ currents [1].

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Knockdown of Nav1.8 caused a significant reduction in mechanical hyperalgesia and allodynia in rat models of inflammatory and neuropathic pain. Suppression of Nav1.8 expression also reduced visceral pain in several experimental models. Activation of Nav1.8 sodium channels primarily drove nociceptor excitability under cold conditions. A rat spinal nerve ligation model of neuropathic pain was used. Oral administration with A 887826 dose-dependently attenuated tactile allodynia in this pain model. The range of free plasma concentrations of A 887826 to produce analgesic efficacy in a spinal nerve ligation model was 3-10 nM. This was consistent with the IC50 value for blocking rat DRG TTX-R sodium currents [1].

Reference:

[1]. Zhang XF, Shieh CC, Chapman ML, et al. A-887826 is a structurally novel, potent and voltage-dependent NaV1.8 sodium channel blocker that attenuates neuropathic tactile allodynia in rats. Neuropharmacology, 2010, 59(3): 201-207.

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