Nelonicline

Cat. No.: HY-16748

CAS No.: 1026134-63-3

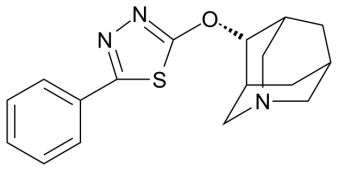
Molecular Formula: $C_{17}H_{19}N_3OS$

Molecular Weight: 313.42

Target: nAChR

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

Storage: 4°C, stored under nitrogen, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 12.5 mg/mL (39.88 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1906 mL	15.9530 mL	31.9061 mL
	5 mM	0.6381 mL	3.1906 mL	6.3812 mL
	10 mM	0.3191 mL	1.5953 mL	3.1906 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: ≥ 1.25 mg/mL (3.99 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (3.99 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (3.99 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Nelonicline (ABT-126) is an orally active and selective α7 nicotinic receptor agonist with high affinity to α7 nAChRs in human brain (K_i=12.3 nM). Nelonicline is used for the research of shizophrenia and Alzheimer's disease[1][2][3].

IC_{50} & Target

Neuronal nicotinic receptor[1]

In Vitro

Nelonicline is an agonist that binds with high affinity to α7 nAChRs in human brain (K_i= 12.3 nM) and activates currents in Xenopus oocytes expressing recombinant human α7 nAChRs (EC_{50}=2 μM; intrinsic activity of 74% relative to acetylcholine). Nelonicline does bind to α3β4* nAChRs in human IMR-32 neuroblastoma cells (K_i=60 nM), but has only 12% efficacy at

100,000 nM in a calcium flux assay in these cell. Like some other α7 nAChR agonists, Nelonicline is also a 5-HT3 receptor antagonist, but it has >10-fold lower affinity for this receptor than for α7 nAChRs (K_i of 140 nM)[1].

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

PROTOCOL

Animal Administration [1]

Monkeys[1]

MPTP-lesioned monkeys are used. All monkeys have been administered MPTP and exhibited mild to moderate parkinsonism. All monkeys are orally gavaged with L-dopa/carbidopa twice daily, which lead to the development of stable abnormal involuntary movements or dyskinesias. The treatment groups are as follows: vehicle-treated (n=6), nicotine-treated (n=5), Nelonicline treated (set 1, n=5) and Nelonicline-treated (set 2, n=5). These latter two sets of monkeys have previously been given ABT-894 and ABT-107 but using somewhat different treatment regimens. The present study is done after a 7 wk washout period, when LIDs are similar in all groups. Nelonicline is administered orally in a small cracker 30 min before L-dopa (10 mg/kg) and carbidopa (2.5 mg/kg). Nicotine, a positive control, is provided in the drinking water. Nelonicline is tested at 0.03, 0.10, 0.30 and 1.0 mg/kg, with each dose of Nelonicline tested for 1 or 2 wk[1].

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

REFERENCES

[1]. Zhang D, et al. α7 nicotinic receptor agonists reduce levodopa-induced dyskinesias with severe nigrostriatal damage. Mov Disord. 2015;30(14):1901-1911.

[2]. Haig G, et al. The α7 Nicotinic Agonist ABT-126 in the Treatment of Cognitive Impairment Associated with Schizophrenia in Nonsmokers: Results from a Randomized Controlled Phase 2b Study. Neuropsychopharmacology. 2016;41(12):2893-2902.

[3]. Gault LM, et al. ABT-126 monotherapy in mild-to-moderate Alzheimer's dementia: randomized double-blind, placebo and active controlled adaptive trial and open-label extension. Alzheimers Res Ther. 2016;8(1):44. Published 2016 Oct 18.

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