Tebanicline dihydrochloride

Cat. No.: HY-14316A

CAS No.: 209326-19-2

Molecular Formula: $C_9H_{13}Cl_3N_2O$

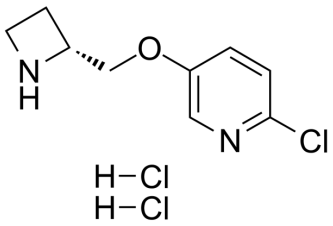
Molecular Weight: 271.57

Target: nAChR

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : 100 mg/mL (368.23 mM; Need ultrasonic)

DMSO : ≥ 34 mg/mL (125.20 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.6823 mL	18.4115 mL	36.8229 mL
5 mM	0.7365 mL	3.6823 mL	7.3646 mL
10 mM	0.3682 mL	1.8411 mL	3.6823 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 25 mg/mL (92.06 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (7.66 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (7.66 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (7.66 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tebanicline dihydrochloride (Ebanicline dihydrochloride) is a nAChR modulator with potent, orally effective analgesic activity. It inhibits the binding of cytisine to α4β2 neuronal nAChRs with a K_i of 37 pM[1].

IC_{50} & Target

Ki: 37 pM (nAChR)[1]

In Vitro	Tebanicline is a novel, potent cholinergic nAChR ligand with analgesic properties that shows preferential selectivity for neuronal nAChRs. It inhibits the binding of cytisine to α4β2 neuronal nAChRs with a K_i of 37 pM. Functionally, tebanicline is an agonist. At the transfected human α4β2 neuronal nAChR in K177 cells, with increased $^{86}Rb^+$ efflux as a measure of cation efflux, ABT-594 has an EC_{50} value of 140 nM with an intrinsic activitycompared with (−)-nicotine of 130%; at the nAChR subtype expressed in IMR-32 cells, an EC_{50} of 340 nM; at the F11 dorsal root ganglion cell line, an EC_{50} of 1220 nM; and via direct measurement of ion currents, an EC_{50} value of 56,000 nM at the human α7 homo-oligimeric nAChR produced in oocytes[1] MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Tebanicline is a potent antinociceptive agent with full efficacy in models of acute and persistent pain and that these effects are mediated predominately by an action at central neuronal nAChRs[2]. Tebanicline produces significant antinociceptive effects in mice against both acute noxious thermal stimulation. ABT-594 is orally active, but 10-fold less potent by this route than after i.p. administration. The antinociceptive effect of ABT-594 is prevented, but not reversed, by the noncompetitive neuronal nicotinic acetylcholine receptor antagonist[3]. Tebanicline has antinociceptive effects in rat models of acute thermal, persistent chemical, and neuropathic pain. Direct injection of tebanicline into the nucleus raphe magnus (NRM) is antinociceptive in a thermal threshold test and destruction of serotonergic neurons in the NRM attenuates the effect of systemic tebanicline[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2][3]	Rats: Rats are dosed with either saline or ABT-594 (0.3 μM/kg i.p.) b.i.d. for 5 days. Treatments are separated by approximately 6 h (i.e., morning and afternoon). In the hot box experiment, animals are tested in the morning and afternoon on days 1, 2 and 5. For each test, a base-line measure is recorded, and then animals are tested 15, 30 and 45 min after treatment. For the afternoon treatment on day 5, all animals received a challenge dose of ABT-594 (0.3 μM/kg i.p.) before being tested. For the motor coordination experiment, animals are tested only in the afternoon on day 5[2]. Mice: Tebanicline is dissolved and diluted in sterile 0.9% saline. The effects of tebanicline are tested for anxiolytic-like activity using the elevated plus-maze procedure. Mice are injected with ABT-594 (0.019, 0.062, or 0.19 μM/kg) or saline, the mouse is placed in the center of the maze and allowed to explore the maze for 5 min. During this period, an auto-mated video tracking system is used to record the time spent on the open arms and the total distance traveled. Diazepam (10.5 μ M/kg, i.p). is used as a positive control compound[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Donnelly-Roberts DL, et al. ABT-594 [(R)-5-(2-azetidinylmethoxy)-2-chloropyridine]: a novel, orally effective analgesic acting via neuronal nicotinic acetylcholine receptors: I. In vitro characterization.J Pharmacol Exp Ther. 1998 May;285(2):777-86.

[2]. Bannon AW, et al. ABT-594 [(R)-5-(2-azetidinylmethoxy)-2-chloropyridine]: a novel, orally effective antinociceptive agent acting via neuronal nicotinic acetylcholine receptors: II. In vivo characterization. J Pharmacol Exp Ther. 1998 May;285(2):787-94.

[3]. Decker MW, et al. Antinociceptive effects of the novel neuronal nicotinic acetylcholine receptor agonist, ABT-594, in mice. Eur J Pharmacol. 1998 Apr 3;346(1):23-33.

[4]. Decker MW, et al. The role of neuronal nicotinic acetylcholine receptors in antinociception: effects of ABT-594. J Physiol Paris. 1998 Jun-Aug;92(3-4):221-4.

Caution: Product has not been fully validated for medical applications. For research use only.

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