Varenicline

Cat. No.:	HY-10019
CAS No.:	249296-44-4
Molecular Formula:	$C_{13}H_{13}N_3$
Molecular Weight:	211.26
Target:	nAChR
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month

SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (118.34 mM; Need ultrasonic)

H_2O : ≥ 20 mg/mL (94.67 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	4.7335 mL	23.6675 mL	47.3350 mL
5 mM	0.9467 mL	4.7335 mL	9.4670 mL
10 mM	0.4734 mL	2.3668 mL	4.7335 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: ≥ 2.5 mg/mL (11.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (11.83 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (11.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Varenicline (CP 526555) is a potent partial agonist for α4β2 nicotinic acetylcholine receptor (nAChR) with an EC_{50} value of 2.3 μM. Varenicline is a full agonist for α3β4 and α7 nAChRs with EC_{50} values of 55 μM and 18 μM, respectively[2]. Varenicline is a nicotinic ligand based on the structure of cytosine, and has the potential for smoking cessation treatment[5].

IC_{50} & Target

EC50: 2.3 μM (α4β2 nAChR); 18 μM (α7 nAChR); 55 μM (α3β4 nAChR)[1]

In Vitro

Varenicline (1 μM, 24 h) inhibits LPS-Induced cytokine secretions (IL-1β, IL-6, and TNF $_{\alpha}$) and cell proliferation rate in RAW 264.7 macrophages[1].
Varenicline (250 nM) evokes action potentials (Aps) in the absence of ACh stimulation in Human adrenal chromaffin cells isolated from male and female organ donors[3].
Varenicline (100 μM, 4 h) promotes migration of HUVECs by lowering the protein expression of VE-cadherin[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	RAW 264.7 murine macrophage cells (treated with 4 μg/mL LPS for 24 h)
Concentration:	1 μM
Incubation Time:	0-48 h
Result:	Decreased the LPS-induced cell proliferation rate.

Western Blot Analysis[4]

Cell Line:	HUVECs
Concentration:	1, 10, 100 μM
Incubation Time:	24 h or 30 min
Result:	Decreased the protein expression of VE-cadherin and activated ERK1/2, p38 and JNK signaling.

In Vivo

Varenicline (Subcutaneous injection, 0.01-1 mg/kg, 3 days) given 10 min prior to nicotine (0.5 mg/kg, s.c.) inhibits nicotine conditioned place preference (CPP)[5].
Varenicline (Subcutaneous injection, 2.5 mg/kg, 3 days) results in a place aversion which is dependent on α5 nAChRs but not β2 nAChRs[5].
Varenicline (Subcutaneous injection, 0.1 and 0.5 mg/kg, 3 days) reverses nicotine withdrawal signs such as hyperalgesia and somatic signs and withdrawal-induced aversion in a dose-related manner[5].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	ICR male mice[5]
Dosage:	0.01-1 mg/kg for 3 days
Administration:	Subcutaneous injection
Result:	Inhibited nicotine conditioned place preference (CPP) in a dose dependent manner.

REFERENCES

[1]. Elif Baris, et al. Varenicline Prevents LPS-Induced Inflammatory Response via Nicotinic Acetylcholine Receptors in RAW 264.7 Macrophages. Front Mol Biosci. 2021 Oct 12;8:721533.

[2]. Mihalak KB, et al. Varenicline is a partial agonist at alpha4beta2 and a full agonist at alpha7 neuronal nicotinic receptors.Mol Pharmacol. 2006 Sep;70(3):801-5. Epub 2006 Jun 9.

[3]. Jin H, et al. Therapeutic concentrations of varenicline in the presence of nicotine increase action potential firing in human adrenal chromaffin cells. J Neurochem. 2017 Jan;140(1):37-52.

[4]. Mitsuhisa Koga, et al. Varenicline promotes endothelial cell migration by lowering vascular endothelial-cadherin levels via the activated α7 nicotinic acetylcholine receptor-mitogen activated protein kinase axis. Toxicology. 2017 Sep 1;390:1-9.

[5]. Bagdas D, et al. New insights on the effects of varenicline on nicotine reward, withdrawal and hyperalgesia in mice.Neuropharmacology. 2018 Aug;138:72-79.

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