Varenicline Hydrochloride

Cat. No.: HY-10020

CAS No.: 230615-23-3

Molecular Formula: $C_{13}H_{14}ClN_3$

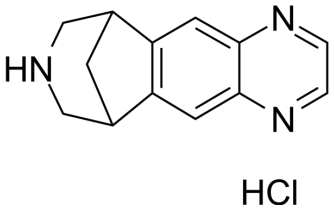
Molecular Weight: 247.72

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 : 50 mg/mL (201.84 mM; Need ultrasonic)

DMSO : ≥ 2.5 mg/mL (10.09 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	4.0368 mL	20.1841 mL	40.3682 mL
	5 mM	0.8074 mL	4.0368 mL	8.0736 mL
	10 mM	0.4037 mL	2.0184 mL	4.0368 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 100 mg/mL (403.68 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Varenicline (CP 526555) is an orally active partial agonist of α4β2 nicotinic acetylcholine receptor (α4β2 nAChR, IC_{50} = 250 nM), which is the principal mediator of nicotine dependence. Varenicline is also a partial agonist of α6β2 nAChR and a full agonist of α6β2 nAChR. Varenicline blocks the direct agonist effects of nicotine on nAChR while stimulates nAChR in a more moderate way, being widely used as an aid of smoking cessation[1][2][3][4][5].

IC_{50} & Target

nAChR[1]

In Vitro

Varenicline (200 μM, 24 h) shows no affection to cell viability of HUVEC cells[3].

Varenicline (100 μM, 24 h) lowers expression of VE-cadherin in HUVEC cells as Varenicline (100 μM, 30 min) significantly activates ERK1/2 and p38 signaling[3].

Varenicline (100 μM, 4 h) promotes migration of HUVEC cells by 2.4-fold[3].

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

Cell Viability Assay[3]

Cell Line:	HUVEC
Concentration:	100, 200, 300, 500 μM
Incubation Time:	24 h
Result:	Did not affect cell viability at 100 and 200 μM (96.8 ± 0.1% and 93.9 ± 1.8%, respectively). Decreased cell viability to 85.7 ± 7.5% and 57.8 ± 7.7% for 300 and 500 μM, respectively.

Western Blot Analysis[3]

Cell Line:	HUVEC
Concentration:	100 μM
Incubation Time:	1, 5, 10, 15 ,30 ,60 min, 24 h
Result:	Significantly activated ERK1/2 and p38 signaling with peak activity at 10–15 min and 10–30 min after treatment, respectively, lowered expression of VE-cadherin at 24 h. MLA (100 nM) significantly reversed the Varenicline-induced effects.

Cell Migration Assay [3]

Cell Line:	HUVEC
Concentration:	100 μM
Incubation Time:	4 h
Result:	Significantly increased the number of migrating cells by 2.4-fold compared with vehicle treatment. MLA (100 nM) completely blocked Varenicline-stimulated migration.

In Vivo

Varenicline (0.5, 1mg/kg, s.c., acute administration) dose-dependently reverses Fentanyl-induced respiratory depression in rats while slightly alleviates Fentanyl-induced sedation[4].
Varenicline (0.004–0.04 mg/kg/h, i.v.drip, 23h a day for 7-10 d) dose-dependently reduces self-administration of nicotine alone (0.0032 mg/kg/inj), and in combination with cocaine (0.0032 mg/kg/inj) with no significant effects on food-maintained responding in cocaine- and nicotine-experienced adult rhesus monkeys[5].
Varenicline (0.178-5.6 mg/kg, i.p., acute administration) shows antidepressant-like activity in the forced swim test in C57BL/6J and CD-1 mice[6].

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Animal Model:	Eighty male Wistar rats (250-300 g)[1]
Dosage:	0.5 mg/kg/day, 1 mg/kg/day or 2 mg/kg/day
Administration:	Subcutaneous injection; twice daily; for 14 days
Result:	Significantly higher DRD2/3 availability in the ventral striatum of approximately 11%, while only the rats treated with 1 and 2 mg/kg/day dose showed significantly higher DRD2/3 availability in the dorsal striatum by 12.5% and 13.2%, respectively.

REFERENCES

[1]. Koegelenberg CF, et al. Efficacy of varenicline combined with nicotine replacement therapy vs varenicline alone for smoking cessation: a randomized clinical trial. JAMA. 2014 Jul;312(2):155-61.

[2]. Magnus CJ, et al. Ultrapotent chemogenetics for research and potential clinical applications. Science. 2019;364(6436):eaav5282.

[3]. Koga M, 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;390:1-9.

[4]. Ren J, et al. Countering Opioid-induced Respiratory Depression in Male Rats with Nicotinic Acetylcholine Receptor Partial Agonists Varenicline and ABT 594. Anesthesiology. 2020 May;132(5):1197-1211.

[5]. Mello NK, et al. Effects of chronic varenicline treatment on nicotine, cocaine, and concurrent nicotine+cocaine self-administration. Neuropsychopharmacology. 2014 Apr;39(5):1222-31.

[6]. Rollema H, et al. Varenicline has antidepressant-like activity in the forced swim test and augments sertraline's effect. Eur J Pharmacol. 2009 Mar 1;605(1-3):114-6.

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