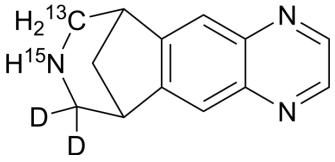
Varenicline-^{15}N,^{13}C,d_2

Cat. No.:	HY-10019S1
Molecular Formula:	$C_{12}{}^{13}CH_{11}D_2N_2{}^{15}N$
Molecular Weight:	215.26
Target:	nAChR; Isotope-Labeled Compounds
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling; Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Varenicline-^{15}N,^{13}C,d_2 is ^{15}N and deuterated labeled Varenicline (HY-10019). 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].
In Vitro	Stable heavy isotopes of hydrogen, carbon, and other elements have been incorporated into drug molecules, largely as tracers for quantitation during the drug development process. Deuteration has gained attention because of its potential to affect the pharmacokinetic and metabolic profiles of drugs[1]. Varenicline (200 μM, 24 h) shows no affection to cell viability of HUVEC cells[4]. 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[4]. Varenicline (100 μM, 4 h) promotes migration of HUVEC cells by 2.4-fold[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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[5]. 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[6]. 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[7]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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.

[7]. Russak EM, et al. Impact of Deuterium Substitution on the Pharmacokinetics of Pharmaceuticals. Ann Pharmacother. 2019 Feb;53(2):211-216.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA