

Encenicline

Catalog No: tcsc0933



Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg



Specifications

CAS No:

550999-75-2

Formula:

$C_{16}H_{17}ClN_2OS$

Pathway:

Neuronal Signaling; Membrane Transporter/Ion Channel

Target:

nAChR; nAChR

Purity / Grade:

>98%

Solubility:

10 mM in DMSO

Alternative Names:

EVP-6124

Observed Molecular Weight:

320.84

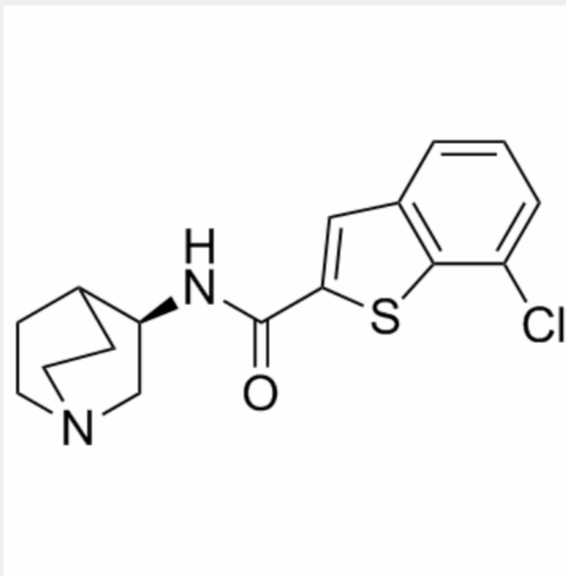
Product Description

Encenicline (EVP-6124) is a novel partial agonist of $\alpha 7$ neuronal nicotinic acetylcholine receptors (**nAChRs**).

IC50 & Target: $\alpha 7$ nAChR^[1]

In Vitro: Encenicline (EVP-6124) displaces [³H]-MLA (Methyllycaconitine) ($K_i=9.98$ nM, $pIC_{50}=7.65\pm 0.06$, $n=3$) and [¹²⁵I]- α -bungarotoxin ($K_i=4.33$ nM, $pIC_{50}=8.07\pm 0.04$, $n=3$). Encenicline (EVP-6124) is approximately 300 fold more potent than the natural agonist ACh ($K_i=3$ μ M), measured in binding assays using [³H]-MLA. Encenicline inhibits the 5-HT₃ receptor by 51% at 10 nM, the lowest concentration tested. Evaluation of the human 5-HT_{2B} receptor expressed in CHO cells demonstrates displacement of [³H]-mesulergine ($K_i=14$ nM) and only antagonist activity in the rat gastric fundus assay at an IC₅₀ of 16 μ M. In binding and functional experiments, Encenicline shows selectivity for $\alpha 7$ nAChRs and does not activate or inhibit heteromeric $\alpha 4\beta 2$ nAChRs^[1].

In Vivo: Encenicline (EVP-6124) has good brain penetration and an adequate exposure time. Encenicline (EVP-6124) (0.3 mg/kg, p.o.) significantly restores memory function in scopolamine-treated rats (0.1 mg/kg, i.p.) in an object recognition task (ORT). Although donepezil at 0.1 mg/kg, p.o. or Encenicline at 0.03 mg/kg, p.o. did not improve memory in this task, co-administration of these sub-efficacious doses fully restored memory. In a natural forgetting test, an ORT with a 24 h retention time, Encenicline improved memory at 0.3 mg/kg, p.o. This improvement is blocked by the selective $\alpha 7$ nAChR antagonist methyllycaconitine (0.3 mg/kg, i.p. or 10 μ g, i.c.v.). Encenicline (EVP-6124) is found to bind moderately to rat plasma proteins with a mean fu of 0.11 ± 0.01 (mean \pm SD) or 11%. Over a range of 0.1-30 mg/kg, p.o., Encenicline (EVP-6124) demonstrates proportional dose escalation. T_{max} is at 4 h in plasma and 2 h brain, although the brain concentrations remained similar between 2 and 8 h. The B:P ratios are 1.7-5.1 between 1 and 8 h^[1]. Pharmacokinetic studies have shown that Encenicline (EVP-6124) (0.4 mg/kg, i.p.) reaches peak brain concentration 2 hr after administration and remains at effective concentrations for at least 4 hr. Encenicline (EVP-6124) is administered to WT mice at ZT0 (0.4 mg/kg i.p single dose) and significantly increases the saturation index of NMDARs in slices obtained 4 hr later without causing prolonged wakefulness or enhanced locomotor activity^[2].



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