

Product Data Sheet

Product Name: EVP-6124 hydrochloride

Cat. No.: GC11091

Chemical Properties

Cas. No. 550999-74-1

Chemical Name N-[(3R)-1-azabicyclo[2.2.2]octan-3-yl]-7-chloro-1-benzothiophene-2-carboxamide;hydrochloride

SMILES C1CN2CCC1C(C2)NC(=O)C3=CC4=C(S3)C(=CC=C4)Cl.Cl

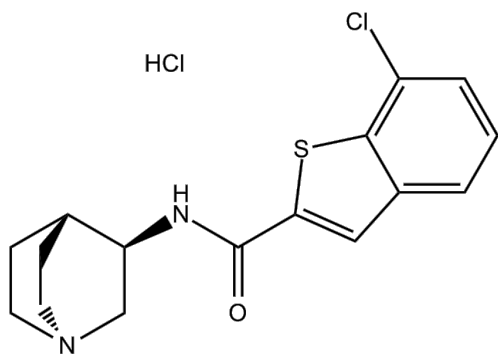
Formula $C_{16}H_{18}Cl_2N_2OS$ M.Wt 357.3

Solubility ≥ 17.9 mg/mL in DMSO, ≥ 100.4 mg/mL in EtOH with gentle warming Storage Store at $-20^{\circ}C$

General tips For obtaining a higher solubility , please warm the tube at $37^{\circ}C$ and shake it in the ultrasonic bath for a while. Stock solution can be stored below $-20^{\circ}C$ for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

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

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**Animal
experiment:**

Rats[1] Twenty-four 2.5-month-old male Wistar rats (average body weight: 329 g) are used. Before testing EVP-6124, the effects of scopolamine alone at 0.03, 0.1, or 0.3 mg/kg, i.p. in the ORT are determined (n=8 per treatment). Scopolamine (0.1 mg/kg, i.p.) injected 30 min before T1 resulted in a robust deficit at T2 when a 1 h interval is used. The d2 index is not significantly different from the chance level of performance; and there are no changes in exploratory behavior for 0.1 mg/kg, i.p. of scopolamine compared with saline. Subsequently, the ability of Encenicline (EVP-6124) to reverse the memory impairment induced by 0.1 mg/kg of scopolamine is tested. First, scopolamine and then Encenicline (EVP-6124) (0.03, 0.1, 0.3, and 1.0 mg/kg, p.o.) are administered 30 min before T1. For the control treatments, animals received either deionized water (p.o.) plus saline (i.p.) or deionized water (p.o.) plus 0.1 mg/kg scopolamine (i.p.). Mice[2] Adult male mice (3-6 months old) are used throughout this study. Encenicline (EVP-6124) is injected i.p. (0.4 mg/kg) at Zeitgeber time (ZT0) in awake mice (9 mice total for this experiment), in the animal facility. Mice are then immediately returned to their home cage with their siblings and left undisturbed for 4 hr (ZT4). During this time, they are closely monitored to check for possible behavioral effects of Encenicline (EVP-6124) injection. All of the 9 injected mice nested and are immobile in the hour following the injection.

References:

- [1]. Prickaerts J, et al. EVP-6124, a novel and selective $\alpha 7$ nicotinic acetylcholine receptor partial agonist, improves memory performance by potentiating the acetylcholine response of $\alpha 7$ nicotinic acetylcholine receptors. *Neuropharmacology*. 2012 Feb;62(2):109
- [2]. Thomas Papouin, et al. Septal Cholinergic Neuromodulation Tunes the Astrocyte-Dependent Gating of Hippocampal NMDA Receptors to Wakefulness. *Neuron*. 2017 May 17;94:1-15.
- [3]. Papouin T, et al. Septal Cholinergic Neuromodulation Tunes the Astrocyte-Dependent Gating of Hippocampal NMDA Receptors to Wakefulness. *Neuron*. 2017 May 17;94(4):840-854.e7.
- [4]. Maehara S, et al. Pharmacological characterization of a novel potent, selective, and orally active phosphodiesterase 2A inhibitor, PDM-631. *Eur J Pharmacol*. 2017 Sep 15;811:110-116.

Background

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EVP-6124 Hydrochloride is a hydrochloride form of EVP-6124. EVP-6124 is partial agonist of $\alpha 7$ neuronal nicotinic acetylcholine receptors (nAChRs) that was proved high-affinity in vitro and in vivo. [1]

EVP-6124 was proved to show selectivity for $\alpha 7$ but low-affinity of $\alpha 4\beta 2$ nAChRs in some binding and functional experiments. EVP-6124 had good brain penetration and an adequate exposure time. [1,2] Co-administration of EVP-6124 and the selective nAChRs antagonist could contribute to the release of DA, ACH, and Glu. This could be used to treat cognitive impairment and possibly other dimensions of psychopathology. Co-administration of donepezil at 0.1 mg/kg, p.o. and EVP-6124 at 0.03 mg/kg proved to be fully restored memory while each of these did not improve memory in this task. [1] Pretreatment with the selective $\alpha 7$ nAChR antagonist, methyllycaconitine (MLA, 1.0 mg/kg), significantly blocked cortical DA and Glu efflux induced by EVP-6124 (0.1 mg/kg). [2,3]

References:

1. Jos Prickaerts, Nick P. van Goethem, et al. *EVP-6124, a novel and selective $\alpha 7$ nicotinic acetylcholine receptor partial agonist, improves memory performance by potentiating the acetylcholine response of $\alpha 7$ nicotinic acetylcholine receptors. Neuropharmacology, 2012,62 (2): 1099-1110.*
2. Mei Huang, Anna R. Felix, et al. Chaya Bhuvaneswaran, Dana Hilt, Gerhard K?nig, Herbert Y. Meltzer, *The alpha-7 receptor agonist EVP-6124 increases dopamine and glutamate efflux in rat medial prefrontal cortex and nucleus accumbens. Biochemical Pharmacology, 2011, 82 (8): 1040.*
3. Mei Huang, Anna R. Felix, et al. *The novel $\alpha 7$ nicotinic acetylcholine receptor agonist EVP-6124 enhances dopamine, acetylcholine, and glutamate efflux in rat cortex and nucleus accumbens. Psychopharmacology, 2014, 231:4541-4551.*

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