
Product Data Sheet

Product Name: EVP-6124

Cat. No.: GC15941

Chemical Properties

Cas. No. 550999-75-2

Chemical Name 7-chloro-N-(quinuclidin-3-yl)benzo[b]thiophene-2-carboxamide

SMILES O=C(C1=CC2=C(C(Cl)=CC=C2)S1)NC(C3)C4CCN3CC4Formula C₁₆H₁₇ClN₂OS M.Wt 320.84

Solubility Soluble in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°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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Kinase experiment:

Binding or activity of EVP-6124 is measured at 10 μM in a selectivity panel according to standard validated protocols under conditions defined by the contractor. For the 5-HT_{2A} receptor binding assay, membranes are prepared from HEK293 cells expressing the human recombinant 5-HT_{2A} receptor. For 5-HT_{2B} and 5-HT_{2C} receptor binding assays, membranes are prepared from CHO cells expressing the human recombinant 5-HT_{2B} or 5-HT_{2C} receptor. Affinity is determined by incubating different concentrations of EVP-6124 in binding buffer for 1 h. For 5-HT_{2A} binding, the incubation is at 22°C in the presence of 0.5 nM [³H]-ketanserin; for 5-HT_{2B}, at 22°C in the presence of 2 nM [³H]-mesulergine; and for 5-HT_{2C}, at 37°C in the presence of 1 nM [³H]-mesulergine. Nonspecific binding is determined in the presence of 1 μM ketanserin, 10 μM mesulergine, or 10 μM RS-102221 for 5-HT_{2A}, 5-HT_{2B}, or 5-HT_{2C}, respectively. All measurements are performed in triplicate. EVP-6124 is also tested in the 5-HT_{2B} rat gastric fundus tissue response assay. Briefly, inhibition of α -methyl serotonin-induced contraction is isometrically measured. All measurements are performed in duplicate[1].

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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 Encenicline, 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 to reverse the memory impairment induced by 0.1 mg/kg of scopolamine is tested. First, scopolamine and then Encenicline (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 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 injection. All of the 9 injected mice nested and are immobile in the hour following the injection.

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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.

Background

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

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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 Bhuvaneshwaran, 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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