
Product Data Sheet

Product Name: (+)-AJ 76 hydrochloride

Cat. No.: GC13156

Chemical Properties

Cas. No. 85379-09-5

Chemical Name (1S,2R)-5-methoxy-1-methyl-N-propyl-1,2,3,4-tetrahydronaphthalen-2-amine hydrochloride

SMILES CCCN[C@]1([H])CCC2=C([C@]1([H])C)C=CC=C2OC.ClFormula $C_{15}H_{23}NO.HCl$ M.Wt 269.81

Solubility Soluble to 10 mM in Water Storage Store at RT

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****Cell experiment [1]:**

Cell lines HEK 293 cells

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

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Preparation Method	Firstly, transient transfection of human D ₃ receptor into HEK 293 cells, 24 hours post-transfection, HEK 293 cells were plated in 12-well cluster dishes and labeled with 10 μ Ci/well (μ Ci is a unit of radioactive activity) of [³ H]-myristic acid for 48h. Then added (+)-A ₁ 76 hydrochloride (1 μ M) for 5min. Finally, PLD (phospholipase D) activity was determined by the transphosphatidylation reaction in the presence of 1% ethanol and (+) 7-OH DPAT (a D ₃ receptor agonist) indicated for 30min at 37°C.
Reaction Conditions	1 μ M; 35min
Applications	D ₃ receptor selective antagonists (+) 7-OH DPAT (a D ₃ receptor agonist) at a concentration of 1 μ M ablated D ₃ receptor-mediated PLD (phospholipase D) activity.
Animal experiment [2]:	
Animal models	MitoPark mice

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The 20-week-old MitoPark mouse were injected with (+)-AJ 76 hydrochloride (20mg/kg) for 60min, then collected the CSF (cerebrospinal fluid) and plasma sample and compared the levels of DOPAC (3,4-Dihydroxyphenylacetic acid) and HVA (homovanillic acid) in CSF samples and the level of HVA in plasma samples between 20-week-old MitoPark mice and their littermate controls at the resting state.

Dosage form

20mg/kg for 60min; i.p. injection

Applications

The levels of HVA in plasma samples of (+)-AJ 76 hydrochloride treated mice were decreased, as were the levels of HVA and DOPA in CSF sample, suggesting that the (+)-AJ 76 hydrochloride can detect Parkinson's disease (PD) at an early stage.

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References:

[1] Everett PB, Senogles SE.

D₃ dopamine receptor activates phospholipase D through a pertussis toxin-insensitive pathway. *Neurosci Lett*. 2004 Nov 16;371(1):34-9. doi: 10.1016/j.neulet.2004.08.033. PMID: 15500962.

[2] Zhou, Jingheng et al. "AJ76 and UH232 as potential agents for diagnosing early-stage Parkinson's disease." *Neuropharmacology* vol. 226 (2023): 109397. doi:10.1016/j.neuropharm.2022.109397.

Background

(+)-AJ 76 hydrochloride is a dopamine receptors (DRs) antagonist^[1] with preferential action at presynaptic receptors (pKi values are 6.95, 6.67, 6.37, 6.21 and 6.07 at hD₃, hD₄, hD_{2S}, hD_{2L} and rD₂ receptors respectively). Dopamine is not only a neurotransmitter involved in motor, cognitive, and reward regulation, but it also plays an immunomodulatory role in the central and peripheral nervous systems^[2]. (+)-AJ 76 hydrochloride can increase extracellular dopamine concentration by blocking presynaptic inhibitory receptors D₂R and/or D₃R on dopaminergic neuron terminals, which promotes dopamine transmission^[3], and is therefore commonly used in neurology and studies of neurological related diseases such as Alzheimer's disease.

In vitro, (+)-AJ 76 hydrochloride (1μM) treatment of HEK 293 cells transfected with the D₃ receptor for 35min reduced cellular phospholipase D (PLD) levels^[4].

In vivo, MitoPark mice treated with intraperitoneal injection (+)-AJ 76 hydrochloride (20mg/kg) for 60 minutes significantly reduced the levels of DOPAC (3,4-Dihydroxyphenylacetic acid) in mouse cerebrospinal fluid and HVA (homovanillic acid) in mouse cerebrospinal fluid and plasma, suggesting that dopamine neuron challenge Test

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(DNC Test) using (+)-AJ 76 hydrochloride is helpful for early detection of PD (Parkinson's disease)^[5]. (+)-AJ 76 hydrochloride (300µmol/kg/day) fed to male Sprague-Dawley rats for 7 days increased voluntary activity activity and DOPAC levels in the striatum^[6].

References:

- [1] Svensson K, Johansson AM, Magnusson T, Carlsson A. (+)-AJ 76 and (+)-UH 232: central stimulants acting as preferential dopamine autoreceptor antagonists. *Naunyn Schmiedeberg's Arch Pharmacol.* 1986 Nov;334(3):234-45. doi: 10.1007/BF00508777. PMID: 2880302.
- [2] Channer, Breana et al. "Dopamine, Immunity, and Disease." *Pharmacological reviews* vol. 75,1 (2023): 62-158. doi:10.1124/pharmrev.122.000618
- [3] Waters N, Lagerkvist S, Löfberg L, Piercey M, Carlsson A. The dopamine D₃ receptor and autoreceptor preferring antagonists (+)-AJ76 and (+)-UH232; a microdialysis study. *Eur J Pharmacol.* 1993 Sep 28;242(2):151-63. doi: 10.1016/0014-2999(93)90075-s. PMID: 8253112.
- [4] Everett PB, Senogles SE. D₃ dopamine receptor activates phospholipase D through a pertussis toxin-insensitive pathway. *Neurosci Lett.* 2004 Nov 16;371(1):34-9. doi: 10.1016/j.neulet.2004.08.033. PMID: 15500962.
- [5] Zhou, Jingheng et al. "AJ76 and UH232 as potential agents for diagnosing early-stage Parkinson's disease." *Neuropharmacology* vol. 226 (2023): 109397. doi:10.1016/j.neuropharm.2022.109397
- [6] Kullingsjö H, Carlsson A, Svensson K. Effects of repeated administration of the preferential dopamine autoreceptor antagonist, (+)-AJ76, on locomotor activity and brain DA metabolism in the rat. *Eur J Pharmacol.* 1991 Dec 3;205(3):241-6. doi: 10.1016/0014-2999(91)90904-5. PMID: 1817961.

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