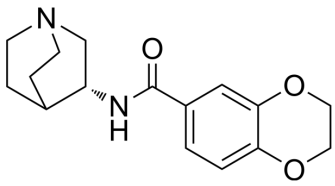
PHA 568487 free base

Cat. No.:	HY-129674
CAS No.:	527680-56-4
Molecular Formula:	$C_{16}H_{20}N_2O_3$
Molecular Weight:	288.34
Target:	nAChR
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (86.70 mM; ultrasonic and warming and adjust pH to 8 with HCl and heat to 80°C)

Preparing Stock Solutions

Mass / Solvent / Concentration	1 mg	5 mg	10 mg
1 mM	3.4681 mL	17.3406 mL	34.6813 mL
5 mM	0.6936 mL	3.4681 mL	6.9363 mL
10 mM	0.3468 mL	1.7341 mL	3.4681 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (7.21 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (7.21 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (7.21 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PHA 568487 free base is a selective alpha 7 nicotinic acetylcholine receptor (α-7 nAchR) agonist. PHA 568487 free base reduces neuroinflammation[1][2][3].

In Vitro

PHA 568487, α-7 nAchR-specific agonist, prevents NF-κb activation in the cells[2].
PHA 568487 treatment significantly reduces the expression of leukocyte infiltration molecules in MCAO rats and in endothelial cells after in vitro ischemia[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

PHA 568487 treatment reduces mouse cognitive decline caused by aseptic bone fracture by promoting inflammation resolution. PHA 568487 (PHA; 0.8 mg/kg; injected intraperitoneally) reduces infarct volume and TUNEL positive neurons in the peri-infarct regions of permanent middle cerebral artery occlusion (pMCAO) and pMCAO+tibia fracture mice[2].
The role played by a7 receptors on neuroinflammation is supported by the decrease of [^{18}F]DPA-714 binding in ischemic rats treated with the a7 agonist PHA 568487 at day 7 after MCAO[3].
PHA 568487-treated ischemic rats show a significant reduction of the cerebral infarct volumes and an improvement of the neurologic outcome compared with non-treated MCAO rats[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57BL/6J male mice (10-12 weeks old) with pMCAO[2]
Dosage:	0.4 and 0.8 mg/kg
Administration:	Injected intraperitoneally once on day 1, or twice on days 1 and 2, after pMCAO
Result:	0.8 mg/kg on days 1 and 2 after pMCAO yielded the best effect on infarct volume and behavior tests.

Animal Model:	Adult male Sprague-Dawley rats[3]
Dosage:	1.25 mg/kg
Administration:	Treated i.p. daily with 0.1 mL
Result:	Showed a significant decrease of [18F]DPA-714 binding in the ischemic cerebral hemisphere in comparison to non-treated ischemic rats.

REFERENCES

[1]. F Barclay Shilliday, et al. Multiple species metabolism of PHA-568487, a selective alpha 7 nicotinic acetylcholine receptor agonist. Drug Metab Lett. 2010 Aug;4(3):162-72.

[2]. Zhenying Han, et al. Alpha-7 nicotinic acetylcholine receptor agonist treatment reduces neuroinflammation, oxidative stress, and brain injury in mice with ischemic stroke and bone fracture. J Neurochem. 2014 Nov;131(4):498-508.

[3]. Lorena Colás, et al. In vivo imaging of A7 nicotinic receptors as a novel method to monitor neuroinflammation after cerebral ischemia. Glia. 2018 Aug;66(8):1611-1624.

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