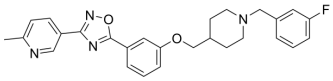
AChE/Nrf2 modulator 1

Cat. No.:	HY-152037
CAS No.:	2417117-84-9
Molecular Formula:	$C_{27}H_{27}FN_4O_2$
Molecular Weight:	458.53
Target:	Cholinesterase (ChE); Keap1-Nrf2
Pathway:	Neuronal Signaling; NF-κB
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

AChE/Nrf2 modulator 1 is an orally active acetylcholinesterase (AChE)/nuclear factor erythroid 2-related factor 2 (Nrf2) modulator. AChE/Nrf2 modulator 1 has Nrf2 inductive activity and AChE inhibitory activity for eeAChE and hAChE with IC_{50} values of 0.07 μM and 0.38 μM, respectively. AChE/Nrf2 modulator 1 can be used for the research of Alzheimer's disease[1].

IC_{50} & Target

IC50: 0.07 μM (eAChE); 0.38 μM (hAChE)[1]

In Vitro

AChE/Nrf2 modulator 1 (Compound 15a) has significant Nrf2 inductivity and excellent AChE inhibitory for eeAChE and hAChE with IC_{50} values of 0.07 μM and 0.38 μM, respectively[1].

AChE/Nrf2 modulator 1 (5, 20 μM; 5-12 h) upregulates the protein and transcription level of Nrf2 and the downstream proteins HO1, NQO1, and GCLM and promotes Nrf2 translocation from cytoplasm into nuclei[1].

AChE/Nrf2 modulator 1 (1, 2.5, 5, 10, 20, 40 μM) exhibits important neuroprotective function in protecting the cells from being damaged by H202 and Aβ1-42 aggregation and exertes antioxidant stress and anti-inflammatory activities in reducing the production of ROS and pro-inflammatory cytokines[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	PC12 cells
Concentration:	20 μM; 5, 20 μM
Incubation Time:	5-10 h; 6 h
Result:	Significantly activated the expression of Nrf2 downstream proteins. Increase the level of Nrf2 and its downstream protein HO-1, NQO1, and GCLM in a dose-dependent manner at 6 h. Increased the translocation of Nrf2 into the nucleus.

RT-PCR[1]

Cell Line:	PC12 cells
Concentration:	20 μM
Incubation Time:	0, 1, 2, 5, 10, 24 h

Result:	Increased the Nrf2, HO-1, NQO1, and GCLM gene expression in dose dependent manner.

Immunofluorescence[1]

Cell Line:	PC12 cells
Concentration:	5, 20 μM
Incubation Time:	12 h
Result:	Induced the Nrf2 translocation into the nucleus in dose dependent manner.

In Vivo

AChE/Nrf2 modulator 1 (Compound 15a) (oral; 10 mg/kg; for 10 consecutive days) effectively shortens the latency time and escape distance to the target, increased the arrival times, and simplified the tracks in Morris water maze test induced by scopolamine and Aβ1-42[1].

AChE/Nrf2 modulator 1 (10, 20 mg/kg; intragastric administration) significantly reduces the levels of proinflammatory factors in the mice model brains[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	ICR mice[1]
Dosage:	10, 20 mg/kg
Administration:	Intragastric administration; oral; for 10 consecutive days
Result:	Significantly reduced the latency time to target and simplified the traveled distance and exhibited a good effect on ameliorating ethological changes and spatial memory impairment by rescuing cholinergic function .Showed an obvious reduction of pro-inflammation factors level and significantly increased the content of TGF-β1.

REFERENCES

[1]. Yuanyuan Wang, et al. Design, synthesis and evaluation of fused hybrids with acetylcholinesterase inhibiting and Nrf2 activating functions for Alzheimer's disease. Eur J Med Chem. 2022 Dec 15;244:114806.

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