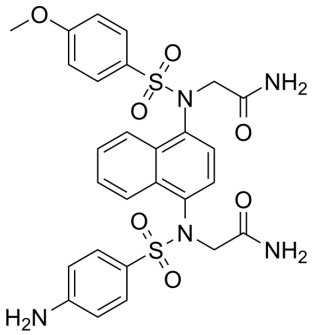
NXPZ-2

Cat. No.:	HY-149010
CAS No.:	2254492-08-3
Molecular Formula:	$C_{27}H_{27}N_5O_7S_2$
Molecular Weight:	597.66
Target:	Keap1-Nrf2
Pathway:	NF-κB
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

NXPZ-2 is an orally active Keap1-Nrf2 protein–protein interaction (PPI) inhibitor with a K_i value of 95 nM, EC_{50} value of 120 and 170 nM. NXPZ-2 can dose-dependently ameliorate $A\beta_{[1-42]}$-Induced cognitive dysfunction, improve brain tissue pathological changes in Alzheimer's disease (AD) mouse by increasing neuron quantity and function. NXPZ-2 can inhibit oxidative stress by increasing Nrf2 expression levels and promoting its cytoplasm to nuclear translocation, which is helpful for Keap1-Nrf2 PPI inhibitors and AD associated disease research[1].

IC_{50} & Target

K_i: 95 nM (Keap 1); EC_{50}: 120 and 170 nM (Keap 1) [1]

In Vitro

NXPZ-2 (0-200 μM, 7 days) has no obvious toxicity on primary cortical neuron[1].

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

Cell Cytotoxicity Assay[1]

Cell Line:	primary cortical neuron
Concentration:	0, 1.6, 8, 40 and 200 μM
Incubation Time:	7 days
Result:	Had no obvious toxicity on primary cortical neuron [1].

In Vivo

NXPZ-2 (Male ICR mice, 52.5/105/210 mg/kg, p.o., once daily for 7 days) improves AD mice learning and memorizing function including increased spontaneous alternation, increases number of active avoidance times, shortened escape latency, increased the time spent in the target quadrant and number of platform crossing[1].

NXPZ-2 (Male ICR mice, 52.5/105/210 mg/kg, p.o., once daily for 7 days) rescues the brain structure damage and lowers dead neuron numbers of AD mice with no obvious toxicity on mouse organs[1].

NXPZ-2 (Male ICR mice, 52.5/105/210 mg/kg, p.o., once daily for 7 days) alleviates oxidative stress by increasing Nrf2 expression levels, and promotes Nrf2's cytoplasm to nuclear translocation, and improves cognitive dysfunction by elevating Nrf2 in both the central nervous system and peripheral blood[1].

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

Animal Model:	Male ICR mice, AD model[1].

Dosage:	52.5 mg/kg, 105 mg/kg, 210 mg/kg.
Administration:	P.o., once daily for 7 days.
Result:	Showed statistically increased spontaneous alternation and no influence on basal motivation, displayed an increased number of active avoidance times, which improved the learning and memory ability of AD mice. Cell number and morphology in NPZX-2-treated groups were restored, dead neuron numbers of AD mice was lowered. Increased serum Nrf2 level, displays more Nrf2 in the hippocampal and cortical nucleus and less expression level in the hippocampal and cortical cytoplasm. Increased Nrf2-ARE binding in both hippocampus and frontal cortex, dose-dependently restored SOD, GSH, and MDA levels, and decreased AD marker protein (p-Tau)[1].

REFERENCES

[1]. Yi Sun, et al. Direct inhibition of Keap1-Nrf2 Protein-Protein interaction as a potential therapeutic strategy for Alzheimer's disease. Bioorg Chem. 2020 Oct;103:104172.

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