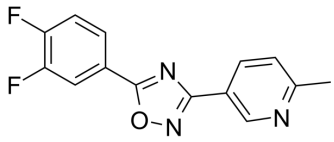
DDO-7263

Cat. No.:	HY-144634
CAS No.:	2254004-96-9
Molecular Formula:	$C_{14}H_9F_2N_3O$
Molecular Weight:	273.24
Target:	Keap1-Nrf2
Pathway:	NF-κB
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 : 17.86 mg/mL (65.36 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.6598 mL	18.2989 mL	36.5979 mL
	5 mM	0.7320 mL	3.6598 mL	7.3196 mL
	10 mM	0.3660 mL	1.8299 mL	3.6598 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 1.79 mg/mL (6.55 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

DDO-7263, a 1,2,4-Oxadiazole derivative, is a potent Nrf2-ARE activator. DDO-7263 upregulates Nrf2 through binding to Rpn6 to block the assembly of 26S proteasome and the subsequent degradation of ubiquitinated Nrf2. DDO-7263 induces Nrf2 translocation into the nucleus. DDO-7263 inhibits of NLRP3 inflammasome activation. DDO-7263 exerts anti-inflammatory activity and has the potential for neurodegenerative diseases research, such as Parkinson's disease (PD)[1][2].

In Vitro

DDO-7263 (20 μM; 2-24 h) can upregulate the protein levels of HO-1 and NQO1 in concentration-dependent manners[1].
DDO-7263 (2.5, 5, 10, 20, 40, 80 μM; 24 h) can upregulate the survival rate of PC12 and THP-Ms cell after 400 μM H_2O_2 in a concentration-dependent manner. DDO-7263 alone has no significant decrease on cell survival rate[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
Incubation Time:	2, 4, 8, 12, 24 hours
Result:	Upregulated the protein levels of HO-1 and NQO1 in concentration-dependent manners.

In Vivo

DDO-7263 (10-100 mg/kg/day; IP; for 10 days) improves the behavioral abnormalities induced by MPTP in mice, significantly attenuates chemically induced dopaminergic neuron loss of tyrosine hydroxylase (TH) in the substantia nigra (SN) and striatum of the mouse brain and inhibits the secretion of inflammatory factors[1].

DDO-7263 (7, 35, 70 mg/kg; IP) has a $T_{1/2}$ of 3.32 hours and a C_{max} of 1.38 mg/mL for rats[1].

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

Animal Model:	Male C57BL/6 mice at 10 weeks of age and body weights of 22-26 g[1]
Dosage:	10, 50, 100 mg/kg
Administration:	IP; daily for 10 days
Result:	Improved the reduction of vertical spontaneous activity and mitigated the loss of balance coordination caused by MPTP (20 mg/kg/day; 7 days). Protected dopaminergic neurons from MPTP. Significantly downregulated the levels of pro-inflammatory factors, including IL-1β and TNF-α, in mouse plasma.

Animal Model:	SD rats[1]
Dosage:	7, 35, 70 mg/kg (Pharmacokinetic Analysis)
Administration:	IP
Result:	Had a $T_{1/2}$ of 3.32 hours and a C_{max} of 1.38 mg/mL.

REFERENCES

[1]. Li-Li Xu, et al. 5-(3,4-Difluorophenyl)-3-(6-methylpyridin-3-yl)-1,2,4-oxadiazole (DDO-7263), a novel Nrf2 activator targeting brain tissue, protects against MPTP-induced subacute Parkinson's disease in mice by inhibiting the NLRP3 inflammasome and protects PC12 cells against oxidative stress. Free Radic Biol Med. 2019 Apr;134:288-303.

[2]. Zhen Dai, et al. Target Fishing Reveals a Novel Mechanism of 1,2,4-Oxadiazole Derivatives Targeting Rpn6, a Subunit of 26S Proteasome. J Med Chem. 2022 Mar 24;65(6):5029-5043.

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