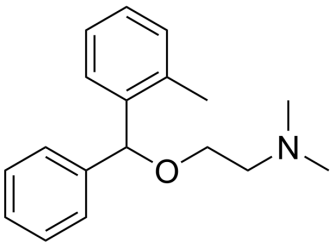
Orphenadrine

Cat. No.:	HY-157959
CAS No.:	83-98-7
Molecular Formula:	$C_{18}H_{23}NO$
Molecular Weight:	269.38
Target:	iGluR; Cytochrome P450; Cholinesterase (ChE)
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling; Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Orphenadrine ((±)-Orphenadrine) is a skeletal muscle relaxant and NMDA antagonist that also has antiparkinsonian, antihistamine, antitremor, antispasmodic, and analgesic effects. Orphenadrine inhibits the binding of $^{[3H]}$MK-801 to the phencyclidine (PCP) binding site of the NMDA receptor. Orphenadrine is also an anticholinergic and cytochrome P450 (CYP) 2B inducer. Orphenadrine may exert pro-tumor effects, causing CAR nuclear translocation, resulting in microsomal reactive oxygen species (ROS) production and oxidative stress. Orphenadrine also exerts neuronal protection, protecting rat cerebellar granule cells (CGC) from 3-NPA-induced death and has inhibitory potential against neurodegenerative diseases mediated by NMDA receptor overactivation[1][2][3].

IC_{50} & Target

NMDA receptor[1]; CYP450 2B[2]; Cholinesterase (ChE)[3]

In Vitro

Orphenadrine (30-300 μM) exhibits relatively fast concentration-dependent open channel blocking kinetics with a K_{off} of 0.013[1].

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

Cell Viability Assay[1]

Cell Line:	NMDA open-channel
Concentration:	30, 100 and 300 μM
Incubation Time:	5 seconds; with 200 μM NMDA
Result:	Nearly completely inhibited $^{[3H]}$MK-801 binding at 100 μM. Exhibited relatively fast, concentration-dependent open channel blocking kinetics.

In Vivo

In a study of the tumor-promoting effects of Orphenadrine, male rats were pretreated with a single intraperitoneal injection of N-diethylnitrosamine (DEN) for 2 weeks. Orphenadrine (0, 750, 1500 ppm; po; 6 wk) accelerates hepatocyte proliferation and induces liver tumor-promoting activity[2].

Orphenadrine (30 mg/kg; po; 3 d) Yes Protect rats from exposure to 3-nitropropionic acid (3-NPA) (30 mg/kg; 3 d), which causes neuronal damage in astrocytes. Markers: [(3)H]-PK 11195 and Increased expression levels of HSP27[3].

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Animal Model:	Liver tumor model in male rats pre-treated by N-diethylnitrosamine[2]

Dosage:	0, 750, 1500 ppm
Administration:	PO; for 6 weeks
Result:	Increased mRNA expression levels of Cyp2b1/2, Mrp2 and Cyclin D1. Increased microsomal reactive oxygen species (ROS) production and oxidative stress markers such as thiobarbituric acid-reactive substances and 8-hydroxydeoxyguanosine.

REFERENCES

[1]. Kornhuber J, et al. Orphenadrine is an uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist: binding and patch clamp studies. J Neural Transm Gen Sect. 1995;102(3):237-46.

[2]. Pubill D, et al. Orphenadrine prevents 3-nitropropionic acid-induced neurotoxicity in vitro and in vivo. Br J Pharmacol. 2001 Feb;132(3):693-702.

[3]. Morita R, et al. Liver tumor promoting effect of orphenadrine in rats and its possible mechanism of action including CAR activation and oxidative stress. J Toxicol Sci. 2013;38(3):403-13.

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