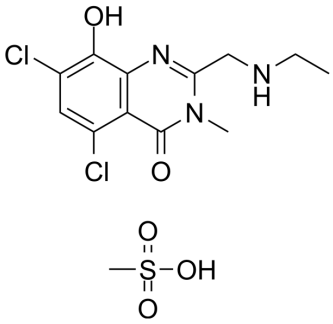
PBT434 mesylate

Cat. No.:	HY-120475A		
CAS No.:	2387898-69-1		
Molecular Formula:	$C_{13}H_{17}Cl_2N_3O_5S$		
Molecular Weight:	398.26		
Target:	α-synuclein		
Pathway:	Neuronal Signaling		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



BIOLOGICAL ACTIVITY

Description

PBT434 methanesulfonate is a potent, orally active and cross the blood-brain barrier α-synuclein aggregation inhibitor. PBT434 methanesulfonate can be used as a iron chelator and modulates transcellular iron trafficking. PBT434 methanesulfonate inhibits iron-mediated redox activity and iron-mediated aggregation of α-synuclein. PBT434 methanesulfonate prevents the loss of substantia nigra pars compacta neurons (SNpc). PBT434 methanesulfonate has the potential for the research of Parkinson's disease (PD)[1][2].

In Vitro

PBT434 methanesulfonate (0-20 μM; 3 h) significantly inhibits H_2O_2 production by iron and significantly reduces the rate of Fe-mediated aggregation of α-synuclein[1].

PBT434 methanesulfonate (0-100 μM; 24 h) shows no cytotoxic effects on brain microvascular endothelial cells[2].

PBT434 methanesulfonate (20 μM; 24 h) incrases the expression of total TfR, Cp protein level in hBMVEC[2].

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

Cell Cytotoxicity Assay[2]

Cell Line:	hBMVEC
Concentration:	1, 10, 20, 50, 100 μM
Incubation Time:	24 h
Result:	Showed no cytotoxic effects on brain microvascular endothelial cells.

Western Blot Analysis[2]

Cell Line:	hBMVEC
Concentration:	20 μM
Incubation Time:	24 h
Result:	Increased the expression of total TfR, Cp protein level.

In Vivo

PBT434 methanesulfonate (30 mg/kg; p.o.; daily for 21 days) significantly preserved neuron numbers in the 6-OHDA intoxication model and shows significantly fewer rotations in the L-DOPA model, significantly reducing SNpc neuronal loss

in the MPTP model[1].

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

Animal Model:	12 weeks, 25 g, Male C57BL/6 J mice (6-OHDA intoxication model)[1]
Dosage:	30 mg/kg
Administration:	P.o.; daily for 21 days (commencing 3 days following induction of lesion)
Result:	Prevented neuronal loss following 6-OHDA, preserving up to 75% of the SNpc neurons remaining (both Nissl and tyrosine hydroxylase (TH) positive neurons) after the initial phase of cell death.

Animal Model:	12 weeks, 25 g, Male C57BL/6 J mice (MPTP model)[1]
Dosage:	1, 3, 10, 30, 80 mg/kg
Administration:	P.o.; daily for 21 days (commenced 24 h after induction of lesion)
Result:	Increased the proportion of SNpc cells rescued, increased there was a trend to improved turning behavior, significantly increased varicosity abundance, prevented the decline in levels of the presynaptic marker synaptophysin (SYNP) in a dose-dependent manner.

REFERENCES

[1]. Finkelstein DI, et al. The novel compound PBT434 prevents iron mediated neurodegeneration and alpha-synuclein toxicity in multiple models of Parkinson's disease. Acta Neuropathol Commun. 2017 Jun 28;5(1):53.

[2]. Bailey DK, Clark W, Kosman DJ. The iron chelator, PBT434, modulates transcellular iron trafficking in brain microvascular endothelial cells. PLoS One. 2021 Jul 26;16(7):e0254794.

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