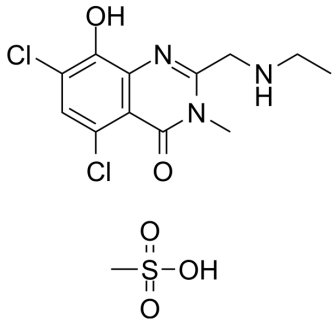
PBT434 mesylate

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:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (251.09 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5109 mL	12.5546 mL	25.1092 mL
	5 mM	0.5022 mL	2.5109 mL	5.0218 mL
	10 mM	0.2511 mL	1.2555 mL	2.5109 mL

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

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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