# PBT434

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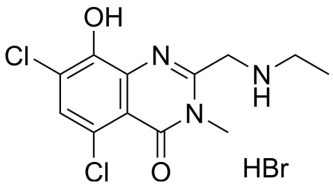
| **Cat. No.:** | HY-120475 |
| **CAS No.:** | 1232841-78-9 |
| **Molecular Formula:** | $C_{12}H_{14}BrCl_2N_3O_2$ |
| **Molecular Weight:** | 383.07 |
| **Target:** | α-synuclein |
| **Pathway:** | Neuronal Signaling |
| **Storage:** | Please store the product under the recommended conditions in the Certificate of Analysis. |




## BIOLOGICAL ACTIVITY

**Description**

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

**In Vitro**

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

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| 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]

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

**In Vivo**

PBT434 (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.

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| 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. |

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| Animal Model: | 12 weeks, 25 g, Male C57BL/6 J mice (6-OHDA intoxication 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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