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Diagnostik & molekulare Diagnostik



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Zuschläge

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SZABO-SCANDIC HandelsgmbH

Quellenstraße 110, A-1100 Wien

T. +43(0)1 489 3961-0

F. +43(0)1 489 3961-7

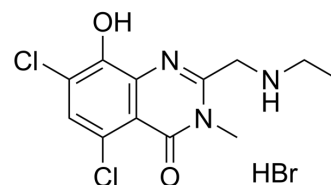
mail@szabo-scandic.com

www.szabo-scandic.com

[linkedin.com/company/szaboscandic](https://www.linkedin.com/company/szaboscandic) 

PBT434

Cat. No.:	HY-120475
CAS No.:	1232841-78-9
Molecular Formula:	C ₁₂ H ₁₄ BrCl ₂ N ₃ O 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	<p>PBT434 (0-20 μM; 3 h) significantly inhibits H₂O₂ production by iron and significantly reduces the rate of Fe-mediated aggregation of α-synuclein^[1].</p> <p>PBT434 (0-100 μM; 24 h) shows no cytotoxic effects on brain microvascular endothelial cells^[2].</p> <p>PBT434 (20 μM; 24 h) increases the expression of total TfR, Cp protein level in hBMVEC^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <p>Cell Cytotoxicity Assay^[2]</p> <table border="1"> <tr> <td>Cell Line:</td> <td>hBMVEC</td> </tr> <tr> <td>Concentration:</td> <td>1, 10, 20, 50, 100 μM</td> </tr> <tr> <td>Incubation Time:</td> <td>24 h</td> </tr> <tr> <td>Result:</td> <td>Showed no cytotoxic effects on brain microvascular endothelial cells.</td> </tr> </table> <p>Western Blot Analysis^[2]</p> <table border="1"> <tr> <td>Cell Line:</td> <td>hBMVEC</td> </tr> <tr> <td>Concentration:</td> <td>20 μM</td> </tr> <tr> <td>Incubation Time:</td> <td>24 h</td> </tr> <tr> <td>Result:</td> <td>Increased the expression of total TfR, Cp protein level.</td> </tr> </table>	Cell Line:	hBMVEC	Concentration:	1, 10, 20, 50, 100 μM	Incubation Time:	24 h	Result:	Showed no cytotoxic effects on brain microvascular endothelial cells.	Cell Line:	hBMVEC	Concentration:	20 μM	Incubation Time:	24 h	Result:	Increased the expression of total TfR, Cp protein level.
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In Vivo	<p>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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>																

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 (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.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA