

Product Data Sheet

Product Name: KYP 2047

Cat. No.: GC50403

Chemical Properties

Cas. No. 796874-99-2

SMILES O=C(N1CCC[C@H]1C#N)[C@@H]2CCCN2C(CCCC3=CC=CC=C3)=O

Formula C₂₀H₂₅N₃O₂

M.Wt 339.44

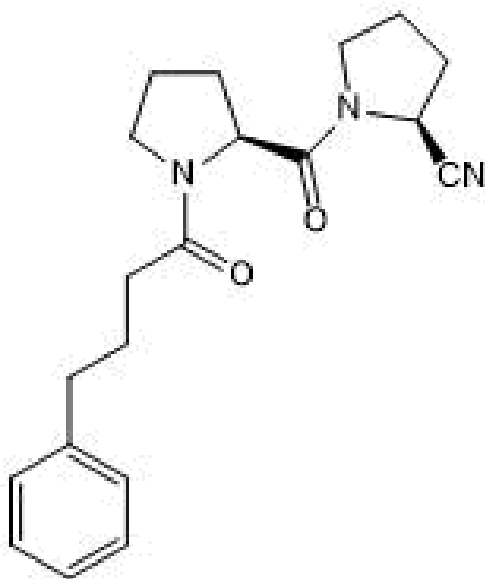
Solubility Soluble in DMSO

Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines U-87 MG, U-138 MG, and A-172 human glioblastoma (GB) cell lines

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Preparation Method GB cells were maintained in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum (FBS), antibiotics, and L-glutamine at 37°C, 5% CO₂. GB cells were treated with KYP 2047 at increasing concentrations (0.01-100μM) for 24 hours.

Reaction Conditions 0.01–100μM; 24 hours

Applications KYP 2047 significantly reduced cell viability in all three GB cell lines in a concentration-dependent manner. KYP 2047 also increased the expression of pro-apoptotic proteins Bax and p53, while decreasing the expression of anti-apoptotic protein Bcl-2. Additionally, KYP 2047 reduced transforming growth factor-β (TGF-β) expression and increased caspase-3 activation.

Animal experiment [2]:

Animal models A30P α-synuclein transgenic mice (Thy1-A30P-α-syn)

Preparation Method Transgenic mice were intraperitoneally administered KYP 2047 (3mg/kg) twice daily for 5 days. Mice were sacrificed after treatment completion for brain tissue analysis.

Dosage form 3mg/kg; i.p.; twice daily for 5 days.

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Applications KYP 2047 treatment significantly reduced α -synuclein immunoreactivity and soluble α -synuclein protein levels in multiple brain regions (striatum, substantia nigra, motor cortex). KYP 2047 also decreased α -synuclein/PREP colocalization and reduced high molecular weight SDS-insoluble α -synuclein oligomers in brain tissues.

[1] Scuderi SA, Casili G, Ardizzone A, et al. KYP-2047, an Inhibitor of Prolyl-Oligopeptidase, Reduces Glioblastoma Proliferation through Angiogenesis and Apoptosis Modulation. *Cancers* (Basel). 2021 Jul 9;13(14):3444.

[2] Myöhänen TT, Hannula MJ, Van Elzen R, et al. A prolyl oligopeptidase inhibitor, KYP-2047, reduces α -synuclein protein levels and aggregates in cellular and animal models of Parkinson's disease. *Br J Pharmacol*. 2012 Jun;166(3):1097-113.

Background

KYP 2047 is a potent, blood-brain barrier permeable prolyl oligopeptidase (POP; $K_i=0.023\text{nM}$) inhibitor. By highly selectively inhibiting POP enzyme activity, KYP 2047 can modulate levels of neuropeptides in the brain that are associated with learning, memory, and neurodegenerative diseases^[1-2]. KYP 2047 can be used in research related to neuropsychiatric disorders such as cognitive impairment, schizophrenia, and Alzheimer's diseases^[3-4].

In vitro, KYP 2047 ($0.01\mu\text{M}$ - $100\mu\text{M}$) treatment of human glioblastoma cells (U-87, A-172, U-138) for 24 hours, KYP 2047 significantly reduced cell viability, upregulated the expression of pro-apoptotic proteins Bax, p53, and caspase-3, while downregulated the expression of anti-apoptotic protein Bcl-2; KYP 2047 inhibited the expression of vascular endothelial growth factor (VEGF), endothelial nitric oxide synthase (eNOS), and transforming growth factor- β (TGF- β), and reduced Matrigel tubule formation^[5]. KYP 2047 ($50\mu\text{M}$ and $100\mu\text{M}$) treatment of tongue squamous cell carcinoma cells (CAL27, HSC-2, HSC-3) for 24 hours, KYP 2047 significantly inhibited cell viability, promoted the expression of Bax, Bad, and caspase-3, reduced the levels of Bcl-2 and mutant p53, and inhibited the expression of VEGF, eNOS, and TGF- β ^[6].

In vivo, KYP 2047 (3mg/kg/day; intraperitoneal injection twice daily) treatment of A30P α -synuclein

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transgenic mice for 5 days, KYP 2047 significantly reduced soluble and insoluble α -synuclein levels in the brain, decreased α -synuclein immunoreactivity and aggregation, and improved neuronal survival^[7]. KYP 2047 (2.5mg/kg/day or 5mg/kg/day; intraperitoneal injection) treatment of bleomycin-induced pulmonary fibrosis mice for 12 days, KYP 2047 significantly alleviated lung tissue fibrosis, collagen deposition, and inflammatory cell infiltration, reduced the expression of pro-fibrotic factors such as TGF- β and VEGF, and modulated the JAK2/STAT3 and NF- κ B signaling pathways^[8].

References:

- [1] Xu P, Bao R, Zhang Y, et al. Prolyl oligopeptidase regulates progesterone secretion via the ERK signaling pathway in murine luteal cells. *Mol Reprod Dev.* 2019 Jun;86(6):714-726.
- [2] Jalkanen AJ, Puttonen KA, Venäläinen JI, et al. Beneficial effect of prolyl oligopeptidase inhibition on spatial memory in young but not in old scopolamine-treated rats. *Basic Clin Pharmacol Toxicol.* 2007 Feb;100(2):132-8.
- [3] Jalkanen AJ, Leikas JV, Forsberg MM. KYP-2047 penetrates mouse brain and effectively inhibits mouse prolyl oligopeptidase. *Basic Clin Pharmacol Toxicol.* 2014 Jun;114(6):460-3.
- [4] Cucinotta L, Palermo N, Ardizzone A, et al. The Inhibition of Prolyl Endopeptidase (PREP) by KYP-2047 Treatment to Reduce Myocardial Ischemia/Reperfusion Injury. *Antioxidants (Basel).* 2025 Apr 8;14(4):442.
- [5] Scuderi SA, Casili G, Ardizzone A, et al. KYP-2047, an Inhibitor of Prolyl-Oligopeptidase, Reduces Glioblastoma Proliferation through Angiogenesis and Apoptosis Modulation. *Cancers (Basel).* 2021 Jul 9;13(14):3444.
- [6] Scuderi SA, Casili G, Filippone A, et al. Beneficial effect of KYP-2047, a propyl-oligopeptidase inhibitor, on oral squamous cell carcinoma. *Oncotarget.* 2021 Dec 7;12(25):2459-2473.
- [7] Myöhänen TT, Hannula MJ, Van Elzen R, et al. A prolyl oligopeptidase inhibitor, KYP-2047, reduces α -synuclein protein levels and aggregates in cellular and animal models of Parkinson's disease. *Br J Pharmacol.* 2012 Jun;166(3):1097-113.
- [8] Cucinotta L, Mannino D, Casili G, et al. Prolyl oligopeptidase inhibition ameliorates experimental pulmonary fibrosis both in vivo and in vitro. *Respir Res.* 2023 Aug 25;24(1):211.

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