

Product Data Sheet

Product Name: TWS119

Cat. No.: GC17868

Chemical Properties

Cas. No. 601514-19-6

Chemical Name 3-[[6-(3-aminophenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]oxy]phenol

SMILES C1=CC(=CC(=C1)N)C2=CC3=C(N2)N=CN=C3OC4=CC=CC(=C4)O

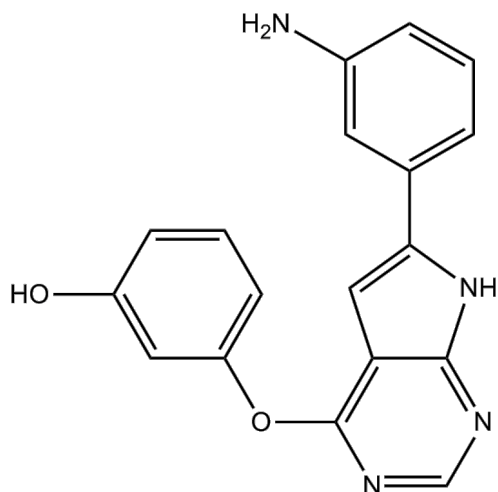
Formula $C_{18}H_{14}N_4O_2$ M.Wt 318.33

Solubility 0.3mg/mL in ethanol, 20mg/mL in DMSO & DMF 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]:

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Cell lines	NK cell line NK-92 or primary NK cellson
Preparation Method	NK cell line NK-92 or primary NK cells were inoculated with TWS119 (2.5μM, 5μM or 20μM) for 48h and then co-cultured with human multiple myeloma RPMI8226 cells for 4h.
Reaction Conditions	2.5, 5 or 20μM,; 48h
Applications	TWS119 concentration-dependently enhanced the degranulation activity, activating-receptor expression, cytotoxicity, and cytokine secretion of NK-92 and primary NK cells when exposed to multiple-myeloma cells.

Animal experiment [2]:

Animal models	Sprague-Dawley (SD) rat
Preparation Method	TWS119 was administrated to the neonatal rats by intraperitoneal injection 20min prior to hypoxia-ischemia (HI) procedure (30mg/kg).
Dosage form	30mg/kg; i.p.; a single administration
Applications	TWS119 performed a neuroprotective function at 7 days after hypoxic-ischemic brain damage via a crosstalk with Wnt/β-catenin and Notch signaling pathways at 24h after hypoxic-ischemic brain damage in neonatal rats.

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- [1] Ren J, Feng X M, Guo Y N, et al. GSK-3 β -catenin pathway plays crucial roles in the regulation of NK cell cytotoxicity against myeloma cells. *FASEB J.* 2023 Mar;37(3):e22821.
- [2] Gao L M, Yang L J, Cui H. GSK-3 β inhibitor TWS119 alleviates hypoxic-ischemic brain damage via a crosstalk with Wnt and Notch signaling pathways in neonatal rats. *Brain Res.* 2021 Oct 1;1768:147588.

Background

TWS119 is a highly potent and selective inhibitor of glycogen synthase kinase-3 β (GSK-3) with K_D value of 126nM and IC_{50} value of 30nM^[1]. TWS119 exerts neuroprotective and regenerative effects, as well as in directing neural differentiation of stem cells and engineering immune cells^{[2][4][6][7]}.

In vitro, TWS119 (5 μ M) pre-incubation on mouse microglial cell line MG6 cells for 1h before stimulated with *Pg*LPS (1 μ g/ml) for 48h significantly decreased mRNA expression of TNF- α and TNF- α secretion induced by *Pg*LPS^[3]. TWS119 (20 μ M, 2.5 μ M or 5 μ M) was applied on NK cell line NK-92 or primary NK cells for 48h. NK cells exhibited a significantly increase in degranulation activity, expression of activating receptors, cellular cytotoxicity, and cytokine secretion when co-cultured with human multiple myeloma RPMI8226 cells for 4h^[4]. TWS119 (0.5, 1.0, 2.0, 4.0, and 8.0 μ M) treatment on $\gamma\delta$ T cells for 72h enhanced the proliferation and survival of $\gamma\delta$ T cells via activation of the mTOR pathway, upregulation of Bcl-2 expression and inhibition of cleaved caspase-3. TWS119 treatment also upregulated the expression of perforin and granzyme B in $\gamma\delta$ T cells and enhanced the cytolytic activity of $\gamma\delta$ T cells against tumour cells^[5].

In vivo, TWS119 (30mg/kg) administrated to the neonatal rats by intraperitoneal injection 20min prior to hypoxia-ischemia (HI) procedure performed a neuroprotective function at 7 days after hypoxic-ischemic brain damage via a crosstalk with Wnt/ β -catenin and Notch signaling pathways at 24h after hypoxic-ischemic brain damage in neonatal rats^[6]. TWS119 (30mg/kg), given intraperitoneally right after rtPA at 4h post-left middle cerebral artery in Sprague–Dawley rats, protects the blood–brain barrier and curbs hemorrhagic transformation by activating Wnt/ β -catenin signaling via GSK-3 β inhibition^[7].

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- [1] Ding, S. Wu T Y H, Brinker A, et al. Synthetic small molecules that control stem cell fate. 2003.Proc. Natl. Acad. Sci. USA 100, 7632–7637.
- [2] Jin F J, Wu Z Z, Hu X, et al. The PI3K/Akt/GSK-3 β /ROS/eIF2B pathway promotes breast cancer growth and metastasis via suppression of NK cell cytotoxicity and tumor cell susceptibility. Cancer Biol Med. 2019 Feb;16(1):38-54.
- [3] Jiang M Z, Zhang X W, Yan X, et al. GSK3 β is involved in promoting Alzheimer's disease pathologies following chronic systemic exposure to Porphyromonas gingivalis lipopolysaccharide in amyloid precursor proteinNL-F/NL-F knock-in mice. Brain Behav Immun. 2021 Nov:98:1-12.
- [4] Ren J, Feng X M, Guo Y N, et al. GSK-3 β / β -catenin pathway plays crucial roles in the regulation of NK cell cytotoxicity against myeloma cells. FASEB J. 2023 Mar;37(3):e22821.
- [5] Chen Y Q, Zheng L, Aldarouish M, et al. Wnt pathway activator TWS119 enhances the proliferation and cytolytic activity of human $\gamma\delta$ T cells against colon cancer. Exp Cell Res. 2018 Jan 1;362(1):63-71.
- [6] Gao L M, Yang L J, Cui H. GSK-3 β inhibitor TWS119 alleviates hypoxic-ischemic brain damage via a crosstalk with Wnt and Notch signaling pathways in neonatal rats. Brain Res. 2021 Oct 1:1768:147588.
- [7] Wang W, Li M C, Wang Y F, et al. GSK-3 β inhibitor TWS119 attenuates rtPA-induced hemorrhagic transformation and activates the Wnt/ β -catenin signaling pathway after acute ischemic stroke in rats. Mol Neurobiol. 2016 Dec;53(10):7028-7036.

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