

Product Data Sheet

Product Name: AXL1717

Cat. No.: GC17045

Chemical Properties

Cas. No. 477-47-4

Chemical Name (5R,5aR,8aS,9R)-5-hydroxy-9-(3,4,5-trimethoxyphenyl)-5a,6,8a,9-tetrahydro-5H-[2]benzofuro[5,6-f][1,3]benzodioxol-8-one

SMILES COC1=CC(=CC(=C1OC)OC)C2C3C(COC3=O)C(C4=CC5=C(C=C24)OCO5)O

Formula $C_{22}H_{22}O_8$

M.Wt 414.41

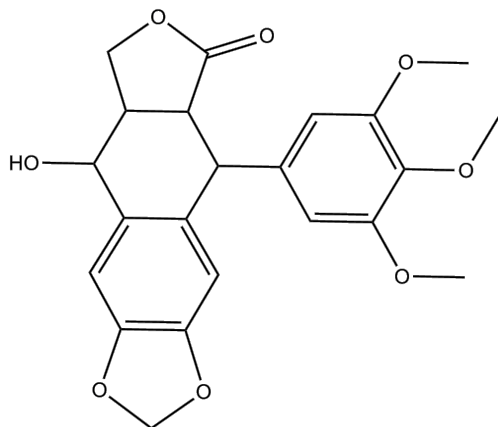
Solubility ≥ 20.7 mg/mL in DMSO

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 BV2 (microglial cell line)

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

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Preparation Method BV2 cells induced by LPS were treated with a combination of 0.2μM AXL1717 and 20μM BA for 24h. After the treatment, the mRNA expression levels of the inflammatory factors IL-1β, IL-6, and TNF-α in BV2 cells were measured by RT-PCR.

Reaction Conditions 0.2μM; 24h

Applications Combined treatment with AXL1717 and BA on LPS-induced BV2 cells significantly enhanced the inhibitory effect of BA on the expression of the inflammatory factors IL-1β, IL-6, and TNF-α.

Animal experiment [1]:

Animal models Pilocarpine-Induced Rat Model

Preparation Method BA was dissolved in sodium carboxymethylcellulose and administered by gavage (80mg/kg) daily after pilocarpine injection. AXL1717 was injected intraperitoneally (0.15mg/day). Seizure frequency, seizure duration, and Racine score were recorded for 1 month in all rats. Survival analysis was performed 1 month later.

Dosage form 0.15mg/day; 30 days; i.p.

Applications Combined treatment with AXL1717 and BA in a pilocarpine-induced epileptic rat model significantly prolonged survival time and reduced seizure frequency, duration, and Racine scores.

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References:

[1] FU P, YUAN Q, SUN Y, et al. Baicalein ameliorates epilepsy symptoms in a pilocarpine-induced rat model by regulation of IGF1R[J]. *Neurochemical Research*, 2020, 45(12): 3021-3033.

Background

AXL1717 is an orally active and highly selective insulin-like growth factor-1 receptor (IGF-1R) inhibitor with an IC_{50} value of 1 nM ^[1]. IGF-1R is a transmembrane tyrosine kinase receptor overexpressed in various human cancers, playing a key role in promoting tumor cell proliferation, inhibiting apoptosis, and enhancing invasive and metastatic capabilities^[2,3]. AXL1717 is commonly used in research related to the IGF-1R signaling pathway and various solid tumors such as malignant astrocytomas and non-small cell lung cancer^[4,5].

In vitro, AXL1717 ($0.2\mu\text{M}$) combined with baicalein (BA) ($20\mu\text{M}$) treatment for 24h in lipopolysaccharide (LPS)-induced BV2 microglial cells significantly enhanced the inhibitory effect of BA on the expression of inflammatory factors IL-1 β , IL-6, and TNF- α ^[6]. AXL1717 ($10\mu\text{M}$) treatment for 48h in high glucose (25mM)-induced human lung cancer A549 cells significantly inhibited high glucose environment-induced cell proliferation and suppressed cell migration ability^[7].

In vivo, AXL1717 (0.15mg/day ; i.p.) combined with BA (80mg/kg ; p.o.) treatment for 30 days in a pilocarpine-induced epileptic rat model significantly prolonged survival time and reduced seizure frequency, duration, and Racine scores^[6]. AXL1717 (40mg/kg ; twice daily; i.p.) administered starting 2h before optic nerve crush surgery for 7 days in CD11b knockout (*Itgam*^{-/-}) mice significantly reduced the area labeled by cholera toxin subunit B (CTB) in the optic nerve, reversing the axonal protective effects brought about by CD11b knockout^[8].

References:

[1] EKMAN S, FRÖDIN J E, HARMENBERG J, et al. Clinical phase I study with an insulin-like growth factor-1 receptor inhibitor: experiences in patients with squamous non-small cell lung carcinoma[J]. *Acta Oncologica*, 2011, 50(3): 441-447.
[2] JIN M, WANG J, BUCK E, et al. Small-molecule ATP-competitive dual IGF-1R and insulin receptor inhibitors: structural insights, chemical diversity and molecular evolution[J]. *Future Medicinal*

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Chemistry, 2012, 4(3): 315-328.

[3] WANG P, MAK V C, CHEUNG L W. Drugging IGF-1R in cancer: New insights and emerging opportunities[J]. Genes & Diseases, 2023, 10(1): 199-211.

[4] AIKEN R, AXELSON M, HARMENBERG J, et al. Phase I clinical trial of AXL1717 for treatment of relapsed malignant astrocytomas: Analysis of dose and response[J]. Oncotarget, 2017, 8(46): 81501.

[5] BERGQVIST M, HOLGERSSON G, BONDARENKO I, et al. Phase II randomized study of the IGF-1R pathway modulator AXL1717 compared to docetaxel in patients with previously treated, locally advanced or metastatic non-small cell lung cancer[J]. Acta Oncologica, 2017, 56(3): 441-447.

[6] FU P, YUAN Q, SUN Y, et al. Baicalein ameliorates epilepsy symptoms in a pilocarpine-induced rat model by regulation of IGF1R[J]. Neurochemical Research, 2020, 45(12): 3021-3033.

[7] FEI J, XIAO C, YANG M, et al. Inhibition of SNCG suppresses the proliferation of lung cancer cells induced by high glucose[J]. Molecular Medicine Reports, 2021, 23(2): 138.

[8] ZHOU J, LIN S, HU Q, et al. Microglial CD11b knockout contributes to axonal debris clearance and axonal degradation attenuation via IGF-1 after acute optic nerve injury[J]. Investigative Ophthalmology & Visual Science, 2023, 64(5): 7.

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