

Product Data Sheet

Product Name: AG-18 (Tyrphostin 23)

Cat. No.: GC17647

Chemical Properties

Cas. No. 118409-57-7

Chemical Name 2-[(3,4-dihydroxyphenyl)methylidene]propanedinitrile

SMILES C1=CC(=C(C=C1C=C(C#N)C#N)O)O

Formula C10H6N2O2

M.Wt 186.17

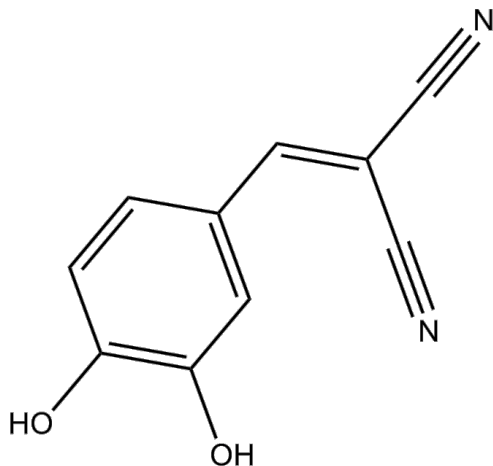
Solubility $\geq 9.3\text{mg/mL}$ in DMSO

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

Primary rat astrocytes

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

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Preparation Method	Primary rat astrocytes were incubated with 100µM AG-18 for 2h, then the extracellular lactate content and glucose consumption were determined using coupled enzymatic assays with lactate dehydrogenase/glutamate pyruvate transaminase and hexokinase/glucose-6-phosphate dehydrogenase, respectively.
Reaction Conditions	100µM; 2h
Applications	Incubation of cultured primary rat astrocytes with 100µM AG-18 for 2h significantly increased lactate release and glucose consumption to 220% and 260% of control values, respectively.
Animal experiment [2]:	
Animal models	NOD-SCID mice bearing LKB1 ^{null} LUAD organoid xenografts
Preparation Method	LKB1 ^{null} LUAD organoids were subcutaneously injected into NOD-SCID mice. After palpable tumours had formed, mice were administered AG-18 (100mg/kg; once daily; per os) for 14 days, and tumour volume was monitored and calculated.
Dosage form	100mg/kg; once daily; 14 days; p.o.
Applications	Treatment with AG-18 resulted in a statistically significant decrease in tumour volume in the absence of LKB1 (60-70% reduction).

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References:[1] Blumrich E M, Kadam R, Dringen R. The protein tyrosine kinase inhibitor tyrphostin 23 strongly accelerates glycolytic lactate production in cultured primary astrocytes[J]. Neurochemical research, 2016, 41(10): 2607-2618.[2] Angelopoulou A, Theocharous G, Valakos D, et al. Loss of the tumour suppressor LKB1/STK11 uncovers a leptin-mediated sensitivity mechanism to mitochondrial uncouplers for targeted cancer therapy[J]. Molecular Cancer, 2024, 23(1): 147.

Background

AG-18 (Tyrphostin 23) is a cell-permeable tyrosine kinase and epidermal growth factor receptor (EGFR) inhibitor, with an IC_{50} of $35\mu M$ for EGFR^[1]. AG-18 blocks receptor autophosphorylation and activation of downstream signaling pathways by acting on the ATP-binding site or substrate-binding site of EGFR^[2]. AG-18 is commonly applied to study EGFR-mediated signal transduction, regulation of cell proliferation, and receptor tyrosine kinase-related mechanisms^[3,4].

In vitro, treatment of primary rat astrocytes with AG-18 ($100\mu M$) for 2h significantly increased lactate release and glucose consumption to 220% and 260% of the control, respectively^[5]. Pretreatment of human alveolar epithelial A549 cells with AG-18 (30, 100, $300\mu M$) for 30min, followed by continued treatment with TNF- α (10ng/mL) for 4.5h, dose-dependently inhibited TNF- α -induced surface expression of intercellular adhesion molecule-1 (ICAM-1)^[6]. Co-incubation of AG-18 ($25-200\mu M$) with mouse striatal homogenate at $30^{\circ}C$ for 2min, using 10nM [^3H]dopamine as the substrate, concentration-dependently inhibited dopamine uptake^[7].

In vivo, LKB1^{null} LUAD organoids were subcutaneously injected into NOD-SCID mice, and after palpable tumors formed, oral administration of AG-18 (100mg/kg; once daily) for 14 days significantly reduced tumor volume (by approximately 60-70%)^[8].

References:

- [1] Boschelli D H. Small molecule inhibitors of receptor tyrosine kinases[J]. Drugs of the Future, 1999, 24(5): 515-538.
- [2] Levitzki A, Gazit A. Tyrosine kinase inhibition: an approach to drug development[J]. Science, 1995, 267(5205): 1782-1788.
- [3] Breen M E, Soellner M B. Small molecule substrate phosphorylation site inhibitors of protein

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kinases: approaches and challenges[J]. ACS chemical biology, 2015, 10(1): 175-189.

[4] Hohnholt M C, Blumrich E M, Waagepetersen H S, et al. The tricarboxylic acid cycle activity in cultured primary astrocytes is strongly accelerated by the protein tyrosine kinase inhibitor tyrphostin 23[J]. Neurochemistry international, 2017, 102: 13-21.

[5] Blumrich E M, Kadam R, Dringen R. The protein tyrosine kinase inhibitor tyrphostin 23 strongly accelerates glycolytic lactate production in cultured primary astrocytes[J]. Neurochemical research, 2016, 41(10): 2607-2618.

[6] Chen C C, Chou C Y, Sun Y T, et al. Tumor necrosis factor α -induced activation of downstream NF- κ B site of the promoter mediates epithelial ICAM-1 expression and monocyte adhesion: involvement of PKC α , tyrosine kinase, and IKK2, but not MAPKs, pathway[J]. Cellular Signalling, 2001, 13(8): 543-553.

[7] Simon J R, Bare D J, Ghetti B, et al. A possible role for tyrosine kinases in the regulation of the neuronal dopamine transporter in mouse striatum[J]. Neuroscience letters, 1997, 224(3): 201-205.

[8] Angelopoulou A, Theocharous G, Valakos D, et al. Loss of the tumour suppressor LKB1/STK11 uncovers a leptin-mediated sensitivity mechanism to mitochondrial uncouplers for targeted cancer therapy[J]. Molecular Cancer, 2024, 23(1): 147.

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