

Product Data Sheet

Product Name: Wortmannin

Cat. No.: GC12338

Chemical Properties

Cas. No. 19545-26-7

Chemical Name (1S,6bR,9aS,11R,11bR)-1-(methoxymethyl)-9a,11b-dimethyl-3,6,9-trioxo-3,6,6b,7,8,9,9a,10,11,11b-decahydro-1H-furo[4,3,2-de]indeno[4,5-h]isochromen-11-yl acetate

SMILES O=C1[C@](C([H])([H])[C@@]2([H])OC(C([H])([H])[H])=O)(C([H])([H])[H])[C@](C([H])([H])C1([H])([H])([H])C(C3=O)=C2[C@]4(C([H])([H])[H])C5=C3OC([H])=C5C(O[C@]4([H])C([H])([H])OC([H])([H])[H])=O

Formula C₂₃H₂₄O₈

M.Wt 428.43

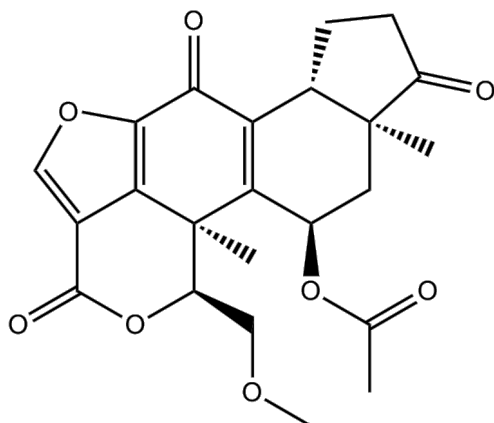
Solubility ≥ 21.42mg/mL in DMSO

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

Kinase experiment [1]:

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For studies of the kinetics of inhibition of PtdIns-3-kinase by wortmannin, bovine brain enzyme was incubated with 0 to 14 nM wortmannin with varying ATP concentrations from 2.5 to 20 μ M. For studies of the time course of PtdIns-3-kinase inhibition, wortmannin 0 to 14 nM, enzyme, and PtdIns were incubated for various times at room temperature before adding [γ -³²P]ATP to start the reaction.

Reaction
Conditions 0-14 nM wortmannin

Applications Kinetic analysis demonstrates that wortmannin is a noncompetitive, irreversible inhibitor of phosphatidylinositol-3-kinase, with inactivation being both time- and concentration-dependent.

Cell experiment [2]:

Cell lines Jurkat cells

Jurkat-soluble fractions were treated with AX7503 (50 nM) for 60 min with or without preincubation with various concentrations of wortmannin (0.25-50 nM) or LY294002 (10-50,000 nM) for 10 min.

Reaction
Conditions Wortmannin (0.25-50 nM) for 10 min

Applications PLK1 activity was inhibited by wortmannin with an IC₅₀ value of 24 nM.

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Animal experiment [3]:

Animal models Scid mice

Preparation Method Oral gavage; daily; in Scid mice; one group of eight mice is dosed with Wortmannin 1 mg/kg for all 14 days. The second group of eight mice is dosed with Wortmannin 1.5 mg/kg for the first 5 days and the dose is decreased to 1 mg/kg for the remaining treatment period.

Dosage form 1 mg/kg for 14 days; 1.5 mg/kg for 5 days + 1.0 mg/kg for 9 days.

Applications Wortmannin treatment significantly slower the growth rate of murine C3H mammary tumor and human MCF-7 breast cancer xenograft. A dose of 1 mg/kg Wortmannin for 7 days decrease the tumor burdens in mice with established murine C3H mammary tumors by 54% relative to controls. Human MCF-7 breast cancer xenograft burdens are decreased by 97% relative to controls after 14 days of 1 mg/kg Wortmannin beginning 1 day after tumor implantation.

References:

- [1]. Powis G, Bonjouklian R, et al. Wortmannin, a potent and selective inhibitor of phosphatidylinositol-3-kinase. *Cancer Res.* 1994 May 1;54(9):2419-23. PMID: 8162590.
- [2]. Liu Y, Shreder KR, et al. Wortmannin, a widely used phosphoinositide 3-kinase inhibitor, also potently inhibits mammalian polo-like kinase. *Chem Biol.* 2005 Jan;12(1):99-107. doi: 10.1016/j.chembiol.2004.11.009. PMID: 15664519.
- [3]. Lemke LE, Paine-Murrieta GD, et al. Wortmannin inhibits the growth of mammary tumors despite the existence of a novel wortmannin-insensitive phosphatidylinositol-3-kinase. *Cancer Chemother Pharmacol.* 1999;44(6):491-7. doi: 10.1007/s002800051123. PMID: 10550570.

Background

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Wortmannin is a potent, selective, and irreversible PI3K inhibitor with an IC₅₀ value of 4.2nM^[1]. Wortmannin is an effective radiosensitizer that irreversibly inhibits DNA-dependent protein kinase (DNA-PK) and ataxia telangiectasia mutated (ATM) with IC₅₀ values of 16nM and 150nM, respectively^[2]. By inhibiting the activity of PI3K, Wortmannin regulates the expression of survivin, cyclinD1, PI3K and p-Akt, and reduces cell migration activity and induces the expression of E-cadherin^[3]. Wortmannin has been widely used to inhibit the secretion of histamine in cells ^[4].

In vitro, Wortmannin treatment for 24 hours significantly inhibited the growth of K562 cells, with an IC₅₀ value of 25nM^[5]. Treatment with 2μM Wortmannin for 24 hours significantly induced apoptosis in MCF-7 cells, accompanied by chromatin condensation, nuclear fragmentation, reactive oxygen species, and membrane blebbing^[6]. Treatment of MDA-MB-231 cells with 200nM Wortmannin for 4 hours significantly inhibited the upregulation of Akt phosphorylation, NF-κB, MMP-9, and IL-8^[7].

In vivo, Wortmannin treatment via oral administration at a dose of 1.5mg/kg/day for 22 days reduced insulin signaling and mortality in seizure-prone Pcmt1^{-/-} mice^[8]. Daily intraperitoneal injection of Wortmannin at a dose of 1mg/kg/day for 28 days significantly inhibited tumor growth in the Colo-699 xenograft mouse model and prolonged the survival time of the mice^[9].

References:

- [1] Walker E H, Pacold M E, Perisic O, et al. Structural determinants of phosphoinositide 3-kinase inhibition by wortmannin, LY294002, quercetin, myricetin, and staurosporine[J]. Molecular cell, 2000, 6(4): 909-919.
- [2] Sarkaria J N, Tibbetts R S, Busby E C, et al. Inhibition of phosphoinositide 3-kinase related kinases by the radiosensitizing agent wortmannin[J]. Cancer research, 1998, 58(19): 4375-4382.
- [3] Bani N, Rahmani F, Shakour N, et al. Wortmannin inhibits cell growth and induces apoptosis in colorectal cancer cells by suppressing the PI3K/AKT pathway[J]. Anti-Cancer Agents in Medicinal Chemistry-Anti-Cancer Agents), 2024, 24(12): 916-927.
- [4] Yano H, Nakanishi S, Kimura K, et al. Inhibition of histamine secretion by wortmannin through the blockade of phosphatidylinositol 3-kinase in RBL-2H3 cells[J]. Journal of Biological Chemistry, 1993, 268(34): 25846-25856.
- [5] Wu Q, Chen Y, Cui G, et al. Wortmannin inhibits K562 leukemic cells by regulating PI3k/Akt channel in vitro[J]. Journal of Huazhong University of Science and Technology [Medical Sciences],

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2009, 29(4): 451-456.

[6] Akter R, Hossain M Z, Kleve M G, et al. Wortmannin induces MCF-7 breast cancer cell death via the apoptotic pathway, involving chromatin condensation, generation of reactive oxygen species, and membrane blebbing[J]. Breast Cancer: Targets and Therapy, 2012: 103-113.

[7] Li J, Li F, Wang H, et al. Wortmannin reduces metastasis and angiogenesis of human breast cancer cells via nuclear factor- κ B-dependent matrix metalloproteinase-9 and interleukin-8 pathways[J]. Journal of International Medical Research, 2012, 40(3): 867-876.

[8] MacKay K B, Lowenson J D, Clarke S G. Wortmannin reduces insulin signaling and death in seizure-prone Pcmt1 $^{-/-}$ mice[J]. 2012.

[9] Boehle A, Kurdow R, Boenicke L, et al. Wortmannin inhibits growth of human non-small-cell lung cancer in vitro and in vivo[J]. Langenbeck's archives of surgery, 2002, 387(5): 234-239.

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