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# 产品名称：GW843682X
# 产品别名：GW843682X

## 生物活性：

**Description**

GW843682X is a selective, ATP-competitive inhibitor of PLK1 and PLK3, with $IC_{50}$s of 2.2 nM and 9.1 nM, respectively, and is also >100-fold selective against ~30 other kinases.

**$IC_{50}$ & Target**

| PLK1 | PLK3 | PDGFR1β | VEGFR2 | Aurora A | CDK2/cyclin A |
|---|---|---|---|---|---|
| 2.2 nM ($IC_{50}$) | 9.1 nM ($IC_{50}$) | 160 nM ($IC_{50}$) | 360 nM ($IC_{50}$) | 4800 nM ($IC_{50}$) | 7600 nM ($IC_{50}$) |

**In Vitro**

GW843682X (compound 1) is effective on inhibition of growth of tumor cells, with IC50s of 0.41, 0.57, 0.11, 0.38, and 0.70 μM for A549, BT474, HeLa, H460 and HCT116 cell lines. GW843682X dose-dependently inhibits PLK1 phosphorylation of Ser15-p53, with an IC50 of 0.14 μM. GW843682X (3 μM) causes a strong G2-M arres in HDF cells and H460 cells after treatment for 24, 48, and 72 h. GW843682X (5 μM) leads to apoptosis in H460 cells instead of HDF cells[1]. GW843682X inhibits proliferation of U937 cells with an EC50 of 120 nM. GW843682X (500 nM) in combination with 5 μM VP-16 suppresses 50% of entry into mitosis in U937 cells[2]. GW843682X (0.06-1 μM) has inhibitory activities against proliferation of acute leukemia cells, and potentiates the anti-proliferative activity of vincristine. Moreover, GW843682X (0.1-1 μM) induces apoptosis of leukemia cells in a dose- and time-dependent manner. GW843682X (0.5-1 μM) dephosphorylates Bcl-xl in leukemia cells[3].

**Solvent&Solubility**

***In Vitro:***

**DMSO : 33.33 mg/mL (69.81 mM;** Need ultrasonic)

**$H_2O$ : < 0.1 mg/mL** (insoluble)

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 2.0944 mL | 10.4721 mL | 20.9442 mL |
| 5 mM | 0.4189 mL | 2.0944 mL | 4.1888 mL |
| 10 mM | 0.2094 mL | 1.0472 mL | 2.0944 mL |

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

***In Vivo:***

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: 2.5 mg/mL (5.24 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (5.24 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

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| | 2.请依序添加每种溶剂： 10% DMSO →90% corn oil<br>Solubility: ≥ 2.5 mg/mL (5.24 mM); Clear solution<br>此方案可获得 ≥ 2.5 mg/mL (5.24 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。 |
| **References** | [1]. Lansing TJ, et al. In vitro biological activity of a novel small-molecule inhibitor of polo-like kinase 1. Mol Cancer Ther. 2007 Feb;6(2):450-9. Epub 2007 Jan 31.<br>[2]. Didier C, et al. Evaluation of Polo-like Kinase 1 inhibition on the G2/M checkpoint in Acute Myelocytic Leukaemia. Eur J Pharmacol. 2008 Sep 4;591(1-3):102-5.<br>[3]. Ikezoe T, et al. A novel treatment strategy targeting polo-like kinase 1 in hematological malignancies. Leukemia. 2009 Sep;23(9):1564-76. |

**实验参考：**

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| **Cell Assay** | Assays are carried out and data analyzed. In these assays, H460 cells are plated at a density of 2,000 per well, HDF cells are plated at 5,000 per well, and the drug-resistant cell line MES-SA/DX5 and its sensitive parent line MES-SA are plated at 7,000 and 6,000 per well, respectively, in a 96-well plate. These densities allowed vehicle controls to grow logarithmically during the course of the 3-day assay. All cells are exposed to 3-fold dilutions of the compound (30-0.00152 μM) in low-glucose DMEM containing 5% FBS, 50 μg/mL gentamicin, and 0.3% (v/v) DMSO (HDF cells); RPMI 1640 containing 5% FBS, 50 μg/mL gentamicin, and 0.3% (v/v) DMSO (H460); or McCoy's 5A containing 5% FBS, 50 μg/mL gentamicin, and 0.3% (v/v) DMSO (MES-SA and MES-SA/DX5)[1]. |
| **Kinase Assay** | PLK1 and PLK3 proteins are prepared from baculovirus-infected Trichoplusia ni cells. Enzyme activity for PLK1 and PLK3 is determined as follows. All measurements are obtained under conditions where signal production increased linearly with time and enzyme. Test compounds are added to white 384-well assay plates (0.1 μL for 10 μL and some 20 μL assays, 1 μL for some 20 μL assays) at variable known concentrations in 100% DMSO. DMSO (1-5% final) and EDTA (65 mM) are used as controls. Reaction Mix containes the following components at 22°C: 25 mM HEPES (pH 7.2); 15 mM $MgCl_2$; 1 μM ATP; 0.05 μCi/well [γ-$^{33}$P]ATP (10 Ci/mmol); 1 μM substrate peptide (Biotin-Ahx-SFNDTLDFD); 0.15 mg/mL bovine serum albumin; 1 mM DTT; and 2 nM PLK1 kinase domain or 5 nM full-length PLK3. Reaction Mix (10 or 20 μL) is quickly added to each well immediately following addition of enzyme via automated liquid handlers and incubated for 1 to 1.5 h at 22°C. The 20 μL enzymatic reactions are stopped with 50 μL of stop mix [50 mM EDTA, 4.0 mg/mL streptavidin SPA beads in Dulbecco's PBS (without $Mg^{2+}$ and $Ca^{2+}$), 50 μM ATP] per well. The 10 μL reactions are stopped with 10 μL of stop mix [50 mM EDTA, 3.0 mg/mL streptavidin-coupled SPA Imaging Beadsin Dulbecco's PBS (without $Mg^{2+}$ and $Ca^{2+}$), 50 μM ATP] per well. Plates are sealed, spun at 500 × g for 1 min or settled overnight, and counted in Packard TopCount for 30 s/well or imaged with a Viewlux imager. Signal above background (EDTA controls) is converted to percent inhibition relative to that obtained in control (DMSO-only) wells[1]. |
| | [1]. Lansing TJ, et al. In vitro biological activity of a novel small-molecule inhibitor of polo-like kinase 1. Mol Cancer Ther. 2007 Feb;6(2):450-9. Epub 2007 Jan 31.<br>[2]. Didier C, et al. Evaluation of Polo-like Kinase 1 inhibition on the G2/M checkpoint in Acute Myelocytic |

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| **References** | Leukaemia. Eur J Pharmacol. 2008 Sep 4;591(1-3):102-5.<br>[3]. Ikezoe T, et al. A novel treatment strategy targeting polo-like kinase 1 in hematological malignancies. Leukemia. 2009 Sep;23(9):1564-76. |