产品名称：**PHA-680632**
产品别名：**PHA-680632**

生物活性：

Description	PHA-680632 is an aurora kinase inhibitor with IC_{50}s of 27, 135 and 120 nM for aurora A, B and C, respectively.		
IC_{50} & Target [1]	Aurora A	Aurora B	Aurora C
	27 nM (IC_{50})	135 nM (IC_{50})	120 nM (IC_{50})
In Vitro	PHA-680632 shows 30- to 200-fold higher IC_{50}s of FLT3, LCK, PLK1, STLK2, VEGFR2, and VEGFR3 compared with Aurora A. PHA-680632 has potent antiproliferative activity in a wide range of cell types. The IC_{50}s are 0.32, 0.41, 0.06, 1.17, 0.56, 0.62, 0.29, 0.11, 1.56, 0.62, 0.07, 0.13, 0.41 μM for C33A, HeLa, HCT116, HT29, LOVO, A549, MCF7, A2780, U2OS, DU145, U937, HL60, NHDF. PHA-680632 can cause polyploidy in tumor cells. PHA-680632 cell treatment induces phenotypes similar to Aurora A or B depletion[1]. PHA680632, inhibits colony formation in different cancer cell lines and induced polyploidy. Aurora-A inhibition by PHA680632 enhances radiation response in cancer cells, especially in p53-deficient cells[2].		
In Vivo	PHA-680632 suppresses tumor growth in animal models. PHA-680632 treatment at 45 mg/kg dose results in 85% of TGI without signs of toxicity in the HL60 human acute myelogenous leukemia xenograft model. PHA-680632 treatment at 60 mg/kg i.v. b.i.d. for 5 days results in 78% of TGI without signs of toxicity in the A2780 human ovarian carcinoma model[1]. PHA680632 in association with radiation leads to an additive effect in cancer cells, especially in the p53-deficient cells, but does not act as a radiosensitiser[2].		

Solvent&Solubility

In Vitro:

DMSO : ≥ 30 mg/mL (59.81 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9935 mL	9.9677 mL	19.9354 mL
	5 mM	0.3987 mL	1.9935 mL	3.9871 mL
	10 mM	0.1994 mL	0.9968 mL	1.9935 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 (4.98 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.98 mM，饱和度未知) 的澄清溶液。

	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。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (4.98 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (4.98 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 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (4.98 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.98 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。 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]. Soncini C, et al. PHA-680632, a novel Aurora kinase inhibitor with potent antitumoral activity. Clin Cancer Res. 2006 Jul 1;12(13):4080-9. [2]. Tao Y, et al. Enhancement of radiation response by inhibition of Aurora-A kinase using siRNA or a selective Aurora kinase inhibitor PHA680632 in p53-deficient cancer cells. Br J Cancer. 2007 Dec 17;97(12):1664-72.

实验参考：

Cell Assay	Cells are seeded at different densities ranging from 5,000 to 15,000 cm^2 in 24-well plate with the appropriate complete medium. After 24 hours, plates are treated with PHA-680632 and incubated for 72 hours at 37°C in 5% CO_2 atmosphere. At the end of incubation time, cells are detached from each plate and counted using a cell counter. IC_{50}s are calculated using percentage of growth versus untreated control [1].
Animal Administration	Mice: Tumour xenograft mice are randomly allocated into four groups (six mice per group): A, control; B, IR alone, 8 Gy in 1 day; C, PHA-680632 alone, 40 mg/kg, b.i.d., for 4 days; D, same dose of PHA-680632 combined with IR (24 h after the first administration of PHA680632, similar schedule as IR alone) for 4 days. Drug or vehicle control (same volume of 20% Tween-80 in 5% glucose solution) is administered intraperitoneally (i.p.). The tumour size is measured twice a week using an electronic caliper. Follow-up of individual mice is conducted. The tumour volume is estimated from 2D tumour measurements[2].
Kinase Assay	Inhibition of kinase activity by PHA-680632 is assessed using a scintillation proximity assay format. In this assay, the biotinylated substrate is transphosphorylated by the kinase in presence of ATP traced with γ^{33}-ATP. The phosphorylated substrate is then captured using streptavidin-coated scintillation proximity assay beads and the extent of phosphorylation is evaluated by β-counter after a 4-hour rest for the floatation of the beads on a dense 5 M CsCl solution. In particular a peptide derived from the Chocktide sequence (LRRWSLGL) is used as substrate for Aurora A, whereas the optimized peptide Auroratide1 is employed for Aurora B and C. The assay is run in a robotized format on 96-well plates. The potency of the compound toward Aurora kinases and 29 additional kinases belonging to our Kinase Selectivity Screening panel is evaluated and the relevant IC_{50}s are determined[1].
	[1]. Soncini C, et al. PHA-680632, a novel Aurora kinase inhibitor with potent antitumoral activity.

References	Clin Cancer Res. 2006 Jul 1;12(13):4080-9. [2]. Tao Y, et al. Enhancement of radiation response by inhibition of Aurora-A kinase using siRNA or a selective Aurora kinase inhibitor PHA680632 in p53-deficient cancer cells. Br J Cancer. 2007 Dec 17;97(12):1664-72.