产品名称：Pirarubicin
产品别名：吡柔比星；THP

生物活性：

Description	Pirarubicin is an anthracycline antibiotics, acts as a topoisomerase II inhibitor, and is a widely used for treatment of various cancers, in particular, solid tumors.
IC_{50} & Target	Topoisomerase II [1]
In Vitro	Pirarubicin is a topoisomerase II inhibitor[1]. Pirarubicin shows inhibitory activities against M5076 and Ehrlich cells, with IC50s of 0.366 and 0.078 μM, respectively. The cytotoxicity of Pirarubicin toward M5076 cells is lower than toward Ehrlich cells, and this is due to the much lower expression of topoisomerase II in M5076 cells than in Ehrlich cells[2]. Pirarubicin (2.5, 5, 10 μg/mL) significantly induces autophagy in a dose dependent manner in bladder cancer (T24, EJ, 5637, J82 and UM-UC-3) cells. Furthermore, Pirarubicin (5 μg/mL) induces apoptosis through inhibition of mTOR/p70S6K/4E-BP1 in bladder cancer cells, and this effect is enhanced by inhibition of autophagy[3].
In Vivo	Pirarubicin (18 mg/kg, i.v.) significantly elevates serum level of BNP, CK-MB, CTnT, LDH, and MDA compared with those in the control group in acute cardiac toxicity rats. Pirarubicin also lowers heart rate, and depresses R-wave voltage, and prolongation of QT intervals in the acute cardiac toxicity model[4].
Solvent&Solubility	***In Vitro:*** **DMSO : 50 mg/mL (79.66 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5933 mL	7.9664 mL	15.9327 mL
	5 mM	0.3187 mL	1.5933 mL	3.1865 mL
	10 mM	0.1593 mL	0.7966 mL	1.5933 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；该产品在溶液状态不稳定，建议您现用现配，即刻使用。

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 (3.98 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (3.98 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。

[1]. Takigawa N, et al. Cytotoxic effect of topoisomerase II inhibitors against adriamycin- and etoposide-resistant small cell lung cancer sublines. Gan To Kagaku Ryoho. 1993 May;20(7):929-35.

[2]. Nagai K, et al. Relationships between the in vitro cytotoxicity and transport characteristics of pirarubicin and doxorubicin in M5076 ovarian sarcoma cells, and comparison with those in Ehrlich ascites carcinoma cells. Cancer Chemother Pharmacol. 2002 Mar;49(3):244-50. Epub 2002 Jan 8.

References	[3]. Li K, et al. Pirarubicin induces an autophagic cytoprotective response through suppression of the mammalian target of rapamycin signaling pathway in human bladder cancer cells. Biochem Biophys Res Commun. 2015 May 1;460(2):380-5. [4]. Wang YD, et al. Cardioprotective effects of rutin in rats exposed to pirarubicin toxicity. J Asian Nat Prod Res. 2017 Oct 27:1-13.

实验参考：

Cell Assay	MTS is used to analyze cell survival. Briefly, cells are plated in 96-well plates in triplicate at 2 × 10^3 cells per well and cultured in growth medium. Then cells are treated with pirarubicin at different concentrations (2.5 μg/mL, 5 μg/mL, 10 μg/mL) for 24 h. MTS reagent (5 mg/mL) is added and incubated at 37°C for 4 h. The absorbance is monitored at 490 nm using a microplate reader[3].
Animal Administration	An acute cardiac toxicity model is established by a single dose of 18 mg/kg pirarubicin through the caudal vein injection. Thirty-six rats are randomized equally to six groups: normal control, cardiac injury (THP) model, dexrazoxane (180 mg/kg), low-dose rutin (25 mg/kg), middle-dose rutin (50 mg/kg), and high-dose rutin (100 mg/kg). Rats in the rutin-treated group are administered different doses of rutin and CMC-Na for 7 days by gavage and a single dose of 18 mg/kg pirarubicin through caudal vein injection. Rats in the dexrazoxane-treated group receive sodium carboxymethylcellulose (CMC-Na) by gavage for six days. 40 mg/kg dexrazoxane is then administered to rats by intraperitoneal injection and 18 mg/kg pirarubicin is administered by caudal vein injection on day 7. Rats in the THP model group receive CMC-Na by gavage for seven days, followed by pirarubicin 18 mg/kg through the caudal vein injection on day 7. Rats in the normal control group receive CMC-Na by gavage for seven days, followed by saline through caudal vein injection on day 7[4].
References	[1]. Takigawa N, et al. Cytotoxic effect of topoisomerase II inhibitors against adriamycin- and etoposide-resistant small cell lung cancer sublines. Gan To Kagaku Ryoho. 1993 May;20(7):929-35. [2]. Nagai K, et al. Relationships between the in vitro cytotoxicity and transport characteristics of pirarubicin and doxorubicin in M5076 ovarian sarcoma cells, and comparison with those in Ehrlich ascites carcinoma cells. Cancer Chemother Pharmacol. 2002 Mar;49(3):244-50. Epub 2002 Jan 8. [3]. Li K, et al. Pirarubicin induces an autophagic cytoprotective response through suppression of the mammalian target of rapamycin signaling pathway in human bladder cancer cells. Biochem Biophys Res Commun. 2015 May 1;460(2):380-5. [4]. Wang YD, et al. Cardioprotective effects of rutin in rats exposed to pirarubicin toxicity. J Asian Nat Prod Res. 2017 Oct 27:1-13.