产品名称：酞胺哌啶酮
产品别名：沙利度胺 ； Thalidomide

生物活性：

Description	Thalidomide is initially promoted as a sedative, inhibits cereblon (CRBN), a part of the cullin-4 E3 ubiquitin ligasecomplex CUL4-RBX1-DDB1, with a K_d of ~250 nM, and has immunomodulatory, anti-inflammatory and anti-angiogenic cancer properties.
IC_{50} & Target	Kd: ~250 nM ($CRL4^{CRBN}$)[1]
In Vitro	Thalidomide is initially promoted as a sedative, has immunomodulatory, anti-inflammatory and anti-angiogenic cancer properties, and targets cereblon (CRBN), a part of the cullin-4 E3 ubiquitin ligase complex CUL4-RBX1-DDB1, with a K_d of ~250 nM[1]. Thalidomide (50 μg/mL) potentiates the anti-tumor activity of icotinib against the proliferation of both PC9 and A549 cells, and this effect is correlated with apoptosis and cell migration. In addition, Thalidomide and icotinib inhibits the EGFR and VEGF-R2 pathways in PC9 cells[3].
In Vivo	Thalidomide (100 mg/kg, p.o.) inhibits the collagen deposition, down-regulates the mRNA expression level of α-SMA and collagen I, and significantly reduces the pro-inflammatory cytokines in RILF mice. Thalidomide alleviates RILF via suppression of ROS and down-regulation of TGF-β/Smad pathway dependent on Nrf2 status[2]. Thalidomide (200 mg/kg, p.o.) combined with icotinib shows synergistic anti-tumor effects in nude mice bearing PC9 cells, suppressing tumor growth and promoting tumor death[3].

Solvent&Solubility

In Vitro:

DMSO : 50 mg/mL (**193.63 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.8725 mL	19.3626 mL	38.7252 mL
	5 mM	0.7745 mL	3.8725 mL	7.7450 mL
	10 mM	0.3873 mL	1.9363 mL	3.8725 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 (9.68 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (9.68 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% corn oil

	Solubility: ≥ 2.5 mg/mL (9.68 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (9.68 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]. Fischer ES, et al. Structure of the DDB1-CRBN E3 ubiquitin ligase in complex with thalidomide. Nature. 2014 Aug 7;512(7512):49-53. [2]. Bian C, et al. Thalidomide (THD) alleviates radiation induced lung fibrosis (RILF) via down-regulation of TGF-β/Smad3 signaling pathway in an Nrf2-dependent manner. Free Radic Biol Med. 2018 Dec;129:446-453. [3]. Sun X, et al. Synergistic Inhibition of Thalidomide and Icotinib on Human Non-Small Cell Lung Carcinomas Through ERK and AKT Signaling. Med Sci Monit. 2018 May 15;24:3193-3203.

实验参考：

Cell Assay	THP-1 cells, A549 cells and KYSE30 cells are cultured in RPMI-1640 Medium supplemented with 10% fetal bovine serum and maintained at 37 °C in an atmosphere of 5% CO_2 and 95% room air. THP-1 cells is irradiated with a single dose of 4 Gy 6-MV X-ray and treated with or without Thalidomide (0.2 μmol/mL)-containing medium for 48 h after radiation. The concentration of Thalidomide is selected based on the preliminary results[2].
Animal Administration	Mice[2] A total of 24 WT C57BL/6 mice are randomly divided into 4 groups for the experiments (n = 6 in each group): a control group, an irradiated group, a group irradiated along with Thalidomide, and a Thalidomide only group. Based on the preliminary results, 100 mg/kg Thalidomide is used in the experiment. Thalidomide is dissolved in DMSO vehicle. The treatment group receives the indicated dose of Thalidomide in 200 μL by gavage every other day beginning on day 1 for six treatments. The control mice receives 200 μL 0.1% DMSO contained-saline only. The lungs are harvested at 12 weeks after irradiation for the analysis. A total of 20 Nrf2-/- mice are randomly divided into 4 groups for the experiments (n = 5 in each group). The experiment procedures of Nrf2-/- mice are the same as WT C57BL/6 mice. In addition, a total of 30 WT C57BL/6 mice are randomly divided into 5 groups for the subsequent experiments (n = 6 in each group): a control group, an irradiated group, a group irradiated along with CDDO-Me and Thalidomide, a group irradiated along with CDDO-Me, and a group irradiated along with Thalidomide. 600 ng and 100 mg/kg are selected as the dose of CDDO-Me and Thalidomide for the experiment, respectively. The treatment group receives the indicated dose of CDDO-Me or Thalidomide in 200 μL by gavage every other day beginning on day 1 for six times. For the combined group of CDDO-Me and Thalidomide, CDDO-Me is delivered in 200 μL by gavage every other day beginning on day 1 for six treatments. Thalidomide is delivered in 200 μL by gavage every other day beginning on day 2 for six treatments[2].
References	[1]. Fischer ES, et al. Structure of the DDB1-CRBN E3 ubiquitin ligase in complex with thalidomide. Nature. 2014 Aug 7;512(7512):49-53. [2]. Bian C, et al. Thalidomide (THD) alleviates radiation induced lung fibrosis (RILF) via down-regulation of TGF-β/Smad3 signaling pathway in an Nrf2-dependent manner. Free Radic Biol Med. 2018 Dec;129:446-453. [3]. Sun X, et al. Synergistic Inhibition of Thalidomide and Icotinib on Human Non-Small Cell Lung Carcinomas Through ERK and AKT Signaling. Med Sci Monit. 2018 May 15;24:3193-3203.