产品名称：**KPT-276**
产品别名：**KPT-276**

生物活性：

Description

KPT-276, analog of KPT-185, is an orally bioavailable selective inhibitors of nuclear export (SINE) that irreversibly bind to CRM1 and block the function of CRM1. IC50 value: Target: CRM1 in vitro: A selective inhibitor of nuclear export compound KPT-276 specifically and irreversibly inhibits the nuclear export function of XPO1. The viability of 12 HMCLs treated with KTP-276 was significantly reduced. KPT-276 also actively induced apoptosis in primary MM patient samples. In gene expression analyses, two genes of probable relevance were dysregulated by KPT-276: cell division cycle 25 homolog A (CDC25A) and bromodomain-containing protein 4 (BRD4), both of which are associated with c-MYC pathway [1]. Inhibition of CRM1 by two novel selective inhibitors of nuclear export (SINE), KPT-185 and KPT-276, in MCL cells resulted in significant growth inhibition and apoptosis induction. KPT-185 also induced CRM1 accumulation in the nucleus, resulting in CRM1 degradation by the proteasome [3]. in vivo: One week after leukemic cell inoculation, the mice were given KPT-276 at 150 mg/kg via oral gavage, 3 times a week, or vehicle control. KPT-276 has the identical CRM1 binding warhead and specificity as KPT-185, similar biologic activity in vitro, but superior oral bioavailability and pharmacokinetics, which allow it to be used in vivo. Mice were monitored for survival. Some mice were killed at day 21 to assess the effects of KPT-276 on leukemia burden by measuring spleen weight and white blood cell count [2]. Oral administration of KPT-276 significantly suppressed tumor growth in an MCL-bearing severe combined immunodeficient mouse model, without severe toxicity [3].

Solvent&Solubility

In Vitro:

DMSO : 20 mg/mL (46.92 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3460 mL	11.7299 mL	23.4599 mL
	5 mM	0.4692 mL	2.3460 mL	4.6920 mL
	10 mM	0.2346 mL	1.1730 mL	2.3460 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 mg/mL (4.69 mM); Clear solution

此方案可获得 ≥ 2 mg/mL (4.69 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.0 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 mg/mL (4.69 mM); Clear solution 此方案可获得 ≥ 2 mg/mL (4.69 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 20.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Ranganathan P, et al. Preclinical activity of a novel CRM1 inhibitor in acute myeloid leukemia. Blood. 2012 Aug 30;120(9):1765-73. [2]. Zhang K, et al. Novel selective inhibitors of nuclear export CRM1 antagonists for therapy in mantle cell lymphoma. Exp Hematol. 2013 Jan;41(1):67-78.e4. [3]. Schmidt J, et al. Genome-wide studies in multiple myeloma identify XPO1/CRM1 as a critical target validated using the selective nuclear export inhibitor KPT-276. Leukemia. 2013 Dec;27(12):2357-65.