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产品名称：CCT241533 (hydrochloride)
产品别名：CCT241533 hydrochloride

生物活性：

Description	CCT241533 hydrochloride is a potent and selective CHK2 inhibitor with an IC_{50} of 3 nM and a K_i of 1.16 nM.	
IC_{50} & Target	Chk2	Chk1
	3 nM (IC_{50})	245 nM (IC_{50})
In Vitro	CCT241533 hydrochloride inhibits CHK2 with an IC_{50} of 3 nM and shows minimal cross reactivity against a panel of kinases at 1 μM. X-ray crystallography confirms that CCT241533 binds to CHK2 in the ATP pocket. CCT241533 blocks CHK2 activity in human tumor cell lines in response to DNA damage, as demonstrated by inhibition of CHK2 autophosphorylation at S516, band-shift mobility changes and HDMX degradation. CCT241533 does not potentiate the cytotoxicity of a selection of genotoxic agents in several cell lines. However, CCT241533 significantly potentiates the cytotoxicity of two structurally distinct PARP inhibitors. Clear induction of the pS516 CHK2 signal is seen with a PARP inhibitor alone and this activation is abolished by CCT241533. The cytotoxicity of CCT241533 in HT-29, HeLa and MCF-7, measured as the growth inhibitory IC_{50}(GI_{50}) by SRB assay, is 1.7, 2.2 and 5.1 μM, respectively[1]. CCT241533 hydrochloride is a potent CHK2 inhibitor (IC_{50}=3 nM), with selectivity (63-fold) over CHK1(IC_{50}=190 nM) and low hERG inhibition (IC_{50}=22 μM)[2].	

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (208.79 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0879 mL	10.4397 mL	20.8794 mL
	5 mM	0.4176 mL	2.0879 mL	4.1759 mL
	10 mM	0.2088 mL	1.0440 mL	2.0879 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 (5.22 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.22 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 (5.22 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.22 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 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 (5.22 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.22 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]. Anderson VE, et al. CCT241533 is a potent and selective inhibitor of CHK2 that potentiates the cytotoxicity of PARP inhibitors. Cancer Res. 2011 Jan 15;71(2):463-72. [2]. Caldwell JJ, et al. Structure-based design of potent and selective 2-(quinazolin-2-yl)phenol inhibitors of checkpoint kinase 2. J Med Chem. 2011 Jan 27;54(2):580-90.

实验参考：

Cell Assay	HT-29, HeLa and MCF-7 cells are exposed to a fixed concentration (GI_{50}) of CCT241533 in combination with increasing concentrations of either PARP inhibitor or cytotoxic drug in a 96 hour SRB assay or 7-10 day colony forming assay. The ability of CCT241533 to enhance cell killing is expressed as a potentiation index (PI) which is the ratio of GI_{50} for the genotoxic or PARP inhibitor alone: GI_{50} for the genotoxic or PARP inhibitor in combination with a CHK2 inhibitor. Thus PI>1 indicates potentiation and PI<1 indicates protection[1].
References	[1]. Anderson VE, et al. CCT241533 is a potent and selective inhibitor of CHK2 that potentiates the cytotoxicity of PARP inhibitors. Cancer Res. 2011 Jan 15;71(2):463-72. [2]. Caldwell JJ, et al. Structure-based design of potent and selective 2-(quinazolin-2-yl)phenol inhibitors of checkpoint kinase 2. J Med Chem. 2011 Jan 27;54(2):580-90.