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产品名称: **PF-670462**
产品别名: **PF-670462**

生物活性:				
Description	PF-670462 is a potent and selective inhibitor of casein kinase (CK1 ϵ and CK1 δ), with IC ₅₀ s of 7.7 nM and 14 nM, respectively.			
IC ₅₀ & Target	CK1 ϵ	CK1 δ	EGFR	SAPK2A/p38
	7.7 nM (IC ₅₀)	14 nM (IC ₅₀)	150 nM (IC ₅₀)	190 nM (IC ₅₀)
In Vitro	PF-670462 is a potent and selective inhibitor of CK1 ϵ and CK1 δ , with IC ₅₀ s of 7.7 nM and 14 nM, respectively. PF-670462 shows less than 30-fold selectivity for EGFR and SAPK2A/p38, with IC ₅₀ s of 150 nM and 190 nM, respectively. PF-670462 also causes a redistribution of the GFP signal to the cytoplasm in a concentration-dependent manner, with an EC ₅₀ of 290 \pm 39 nM in CK1 ϵ -transfected COS7 cells[1]. PF-670462 is a potent inhibitor of Wnt/ β -catenin signaling, with an IC ₅₀ of \sim 17 nM. PF-670462 (1 μ M) is a weak inhibitor of proliferation, and only modestly suppresses the growth of HEK293 and HT1080 cells. PF-670462 (100 nM) strongly inhibits CK1 ϵ and CK1 δ , consistent with its effect on Wnt/ β -catenin signaling[2].			
In Vivo	PF-670462 (50 mg/kg, s.c.) produces robust phase delays, and the activity remains persistent, with no discernible correction in the absence of exogenous zeitgebers in rats. PF-670462 (25, 50, and 100 mg/kg, s.c.) induces dose-dependent phase shift[1]. PF-670462 (50 mg/kg; s.c.) significantly phase delays the rhythmic transcription of Bmal1, Per1, Per2 and Nr1d1 in both liver and pancreas by 4.5 \pm 1.3 h and 4.5 \pm 1.2 h, respectively, 1 day after administration. In the suprachiasmatic nucleus (SCN), the rhythm of Nr1d1 and Dbp mRNA expression is also delayed by 4.2 and 4 h, respectively[3].			
Solvent&Solubility	In Vitro: DMSO : \geq 32 mg/mL (77.99 mM) * " \geq " means soluble, but saturation unknown.			
	Preparing Stock Solutions	Solvent Mass Concentration	1 mg	5 mg
		1 mM	2.4371 mL	12.1856 mL
		5 mM	0.4874 mL	2.4371 mL
		10 mM	0.2437 mL	1.2186 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			



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	<p>Solubility: ≥ 2.08 mg/mL (5.07 mM); Clear solution</p> <p>此方案可获得 ≥ 2.08 mg/mL (5.07 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 μL 20.8 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。</p> <p>2. 请依序添加每种溶剂: 10% DMSO \rightarrow 90% (20% SBE-β-CD in saline)</p> <p>Solubility: ≥ 2.08 mg/mL (5.07 mM); Clear solution</p> <p>此方案可获得 ≥ 2.08 mg/mL (5.07 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 μL 20.8 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。</p>
References	<p>[1]. Badura L, et al. An inhibitor of casein kinase I epsilon induces phase delays in circadian rhythms under free-running and entrained conditions. J Pharmacol Exp Ther. 2007 Aug;322(2):730-8. Epub 2007 May 14.</p> <p>[2]. Cheong JK, et al. IC261 induces cell cycle arrest and apoptosis of human cancer cells via CK1δ? and Wnt/β-catenin independent inhibition of mitotic spindle formation. Oncogene. 2011 Jun 2;30(22):2558-69.</p> <p>[3]. Kennaway DJ, et al. Acute inhibition of casein kinase 1δ/ϵ rapidly delays peripheral clock gene rhythms. Mol Cell Biochem. 2015 Jan;398(1-2):195-206.</p>
实验参考:	
Animal Administration	<p>Adult male CD rats (initial weight 175-225 g) are released into constant darkness (DD) for 2 weeks, and their individual free-running periods and times of activity onset are determined from the 7 to 10 days at the end of the 2-week period. Dosing of 50 mg/kg PF-670462 or vehicle (40% β-cyclodextrin) takes place at circadian time (CT)9 or 3 h before the predicted onset of activity; night vision goggles facilitated the subcutaneous administration. CT9 is chosen based on preliminary data demonstrating robust responses to CK1ϵ inhibition at this circadian time. Animals are maintained under DD for an additional 4 to 5 days postdose, and the data from that time period are used in the estimation of the magnitude and direction of the putative phase shifts[1].</p>
Kinase Assay	<p>The CK1ϵ kinase assay is performed in a 40-μL final volume in buffer containing 50 mM Tris, pH 7.5, 10 mM MgCl₂, 5 mM dithiothreitol with 5 μM ATP, 3 nM CK1$\epsilon$$\Delta$319, and 15 μM peptide substrate PLSRTLpSVASLPGL in the presence of 5 μL of CK1ϵ inhibitor (PF-670462) or 5% dimethyl sulfoxide. The reaction is incubated for 3 h at 27°C; detection is carried out as described for the Kinase-Glo Assay. Luminescent output is measured[1].</p>
References	<p>[1]. Badura L, et al. An inhibitor of casein kinase I epsilon induces phase delays in circadian rhythms under free-running and entrained conditions. J Pharmacol Exp Ther. 2007 Aug;322(2):730-8. Epub 2007 May 14.</p> <p>[2]. Cheong JK, et al. IC261 induces cell cycle arrest and apoptosis of human cancer cells via CK1δ? and Wnt/β-catenin independent inhibition of mitotic spindle formation. Oncogene. 2011 Jun 2;30(22):2558-69.</p> <p>[3]. Kennaway DJ, et al. Acute inhibition of casein kinase 1δ/ϵ rapidly delays peripheral clock gene rhythms. Mol Cell Biochem. 2015 Jan;398(1-2):195-206.</p>