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产品名称：7-[2-(环丙基甲氧基)-6-羟基苯基]-1,4-二氢-5-[(3S)-3-哌啶基]-2H-吡啶并[2,3-D][1,3]恶嗪盐酸盐
产品别名：Bay 65-1942 hydrochloride

生物活性：

Description	Bay 65-1942 hydrochloride is an ATP-competitive and selective IKKβ inhibitor.
IC_{50} & Target	IKKβ
In Vitro	Delivery of Bay 65-1942 prior to ischemia significantly decreases left ventricular infarct size compared with animals receiving vehicle. Compared with sham animals, animals receiving vehicle have a significant increase in the infarct-to-area at risk (AAR) ratio (70.7±3.4 vs. 5.8±3.4%, P<0.05). This ratio is significantly reduced by treatment with Bay 65-1942 at each time point (prior to ischemia 42.7±4.1%, at reperfusion 42.7±7.5%, 2 h of reperfusion 29.4±5.2%; each group P<0.05 vs. vehicle). Animals pretreated with Bay 65-1942 (n=3) have significantly attenuated CK-MB levels compared with those animals without treatment prior to IR (14,170 ±3,219 units, P<0.05 vs. vehicle)[1].
In Vivo	Inhibitors of MEK (AZD6244) and IKK (BAY 65-1942) are used at their IC50 concentrations, as determined by a 48 hour MTS assay, which achieve sufficient inhibition of kinase activity. MYL-R cells are treated for 24 hours with AZD6244 (5 μM), BAY 65-1942 (10 μM), or a combination of these inhibitors at the same concentrations. AZD6244 and BAY 65-1942 demonstrate synergistic inhibition of cell viability at the dose combination (5 μM AZD6244+10 μM BAY 65-1942), which correlates with IC75 (CI = 0.48±0.01). Synergism is also indicated at the IC50 (CI = 0.56±0.09) and IC90 (CI = 0.46±0.02) dose combinations reported by the software (CI values are the mean of three independent experiments, ± standard deviation). AZD6244 and BAY 65-1942 treatment induces 2- and 1.3-fold caspase 3/7 activation, respectively, compared to the DMSO-treated cells. Treatment with a combination of AZD6244 plus BAY 65-1942 leads to a 3.2-fold increase in caspase 3/7 activity[2].
Solvent&Solubility	***In Vitro:*** **DMSO : 50 mg/mL (115.76 mM;** Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3153 mL	11.5765 mL	23.1530 mL
5 mM	0.4631 mL	2.3153 mL	4.6306 mL
10 mM	0.2315 mL	1.1576 mL	2.3153 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 (5.79 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.79 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 (5.79 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.79 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 (5.79 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.79 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]. Inhibition of IκB kinase-β protects dopamine neurons against lipopolysaccharide-induced neurotoxicity By Zhang, Feng; Qian, Li; Flood, Patrick M.; Shi, Jing-Shan; Hong, Jau-Shyong; Gao, Hui-Ming J Pharmacol Exp Ther. 2010 June; 333(3): 822-833. [2]. Cooper MJ, et al. Application of multiplexed kinase inhibitor beads to study kinome adaptations in drug-resistant leukemia. PLoS One. 2013 Jun 24;8(6):e66755.

实验参考：

Cell Assay	Cell viability is determined by seeding MYL-R cells on a 96-well plate at 4×10^4 cells/well in 100 μL RPMI growth medium supplemented with kinase inhibitors. Growth media and kinase inhibitors are replenished at 24 hours, and at 48 hours. 20 μL of MTS assay reagent is added to each well. The plate is returned to the incubator for approximately 1 hour and the absorbance at 490 nm is recorded. For combination index (CI) experiments, cells are grown and assayed. To determine AZD6244 and BAY 65-1942 (10 μM) dose-effects, cells are treated with a series of three-fold dilutions of each drug singly, or in combination while maintaining a constant ratio of 1:2, respectively. Cell viability results are analyzed to derive CI values. The CI values from three independent experiments are averaged[2].
Animal Administration	Mice[1] Male C57BL/6 mice, 8-10 wk of age are used. To investigate IKKβ inhibition in myocardial IR injury, mice are subjected to 30 min of cardiac ischemia followed by varying periods of reperfusion. An intraperitoneal injection of Bay 65-1942 (5 mg/kg) at appropriate dosing time points is administered. Nontreatment groups receive a vehicle of 10% cremaphor in water. In treatment groups, Bay 65-1942 is delivered either prior to ischemia, at the time of reperfusion, or 2 h after reperfusion injury. Infarct size is measured 24 h after reperfusion injury in sham, vehicle, and each treatment group. To confirm myocardial injury, serum creatine kinase-muscle-brain fraction (CK-MB)

	levels are measured 1 h after reperfusion in animals pretreated with Bay 65-1942.
References	[1]. Inhibition of IκB kinase-β protects dopamine neurons against lipopolysaccharide-induced neurotoxicity By Zhang, Feng; Qian, Li; Flood, Patrick M.; Shi, Jing-Shan; Hong, Jau-Shyong; Gao, Hui-Ming J Pharmacol Exp Ther. 2010 June; 333(3): 822-833. [2]. Cooper MJ, et al. Application of multiplexed kinase inhibitor beads to study kinome adaptations in drug-resistant leukemia. PLoS One. 2013 Jun 24;8(6):e66755.