产品名称：Ro 31-8220 Mesylate
产品别名：Ro 31-8220 mesylate

生物活性：

Description

Ro 31-8220 mesylate is a potent **PKC** inhibitor, with **IC_{50}**s of 5, 24, 14, 27, 24 and 23 nM for PKCα, PKCβI, PKCβII, PKCγ, PKCε and rat brain PKC, respectively. Ro 31-8220 also significantly inhibits MAPKAP-K1b, MSK1, S6K1 and GSK3β (**IC_{50}**s, 3, 8, 15, and 38 nM, respectively), with no effect on MKK3, MKK4, MKK6 and MKK7.

IC_{50} & Target

PKC-α	PKC-βI	PKC-βII	PKC-γ	PKC-ε
5 nM (IC_{50})	24 nM (IC_{50})	14 nM (IC_{50})	27 nM (IC_{50})	24 nM (IC_{50})
Rat Brain PKC	MAPKAP-K1b	MSK1	S6K1	GSK3β
23 nM (IC_{50})	3 nM (IC_{50})	8 nM (IC_{50})	15 nM (IC_{50})	38 nM (IC_{50})

In Vitro

Ro 31-8220 mesylate is a potent PKC inhibitor, with IC50s of 5, 24, 14, 27, 24 and 23 nM for PKCα, PKCβI, PKCβII, PKCγ, PKCε and rat brain PKC, respectively[1]. Ro 31-8220 also significantly inhibits MAPKAP-K1b, MSK1, S6K1 and GSK3β (IC50s, 3, 8, 15, and 38 nM, respectively), with no effect on MKK3, MKK4, MKK6 and MKK7. Moreover, Ro 31-8220 directly suppresses voltage-dependent Na+ channels[2]. Ro 31-8220 (1 μM) is neuroprotective against paraoxon-induced neuronal cell death in cerebellar granule neurons, blocks paraoxon-induced caspase-3 activity, and reduces the paraoxon-induced increase in phospho-PKC pan levels[3].

In Vivo

Ro 31-8220 (6 mg/kg/d, s.c.) is well tolerated, and has half-life of 5.7 hours in mice. Ro 31-8220-treated MLP−/− mice show a dramatic rescue in fractional shortening after treatment for 6 weeks, but the WT mice shows no change[4].

Solvent&Solubility

In Vitro:

DMSO : ≥ 50 mg/mL (90.31 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8062 mL	9.0310 mL	18.0620 mL
5 mM	0.3612 mL	1.8062 mL	3.6124 mL
10 mM	0.1806 mL	0.9031 mL	1.8062 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 (4.52 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (4.52 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 (4.52 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.52 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。
References	[1]. Wilkinson SE, et al. Isoenzyme specificity of bisindolylmaleimides, selective inhibitors of protein kinase C. Biochem J. 1993 Sep 1;294 (Pt 2):335-7. [2]. Davies SP, et al. Specificity and mechanism of action of some commonly used protein kinase inhibitors. Biochem J. 2000 Oct 1;351(Pt 1):95-105. [3]. Tian F, et al. Inhibition of protein kinase C protects against paraoxon-mediated neuronal cell death. Neurotoxicology. 2007 Jul;28(4):843-9. Epub 2007 Apr 20. [4]. Hambleton M, et al. Pharmacological- and gene therapy-based inhibition of protein kinase Calpha/beta enhances cardiac contractility and attenuates heart failure. Circulation. 2006 Aug 8;114(6):574-82.

实验参考：

Cell Assay	A neurotoxic concentration of paraoxon (200 μM) is added to the granule cell cultures for the indicated time on day in vitro (DIV) 8. The following drugs are added to the granule cell cultures prior to or after paraoxon exposure on DIV 8: Ro-81-3220 (1 μM) is added 15 min prior to or 3 h after the addition of paraoxon. TPA (0.1 μM) is added 15 min prior to the addition of paraoxon[1].
Animal Administration	Mice[4] The affects of long-term Ro 31-8220 administration over 4 to 6 weeks in MLP−/− heart failure mice are investigated. All mice are assessed for ventricular performance by echocardiography at the beginning of the study and 6 weeks later. Ro 31-8220 (or vehicle) is injected subcutaneously once per day at a dosage of 6 mg/kg/d[4].
References	[1]. Wilkinson SE, et al. Isoenzyme specificity of bisindolylmaleimides, selective inhibitors of protein kinase C. Biochem J. 1993 Sep 1;294 (Pt 2):335-7. [2]. Davies SP, et al. Specificity and mechanism of action of some commonly used protein kinase inhibitors. Biochem J. 2000 Oct 1;351(Pt 1):95-105. [3]. Tian F, et al. Inhibition of protein kinase C protects against paraoxon-mediated neuronal cell death. Neurotoxicology. 2007 Jul;28(4):843-9. Epub 2007 Apr 20. [4]. Hambleton M, et al. Pharmacological- and gene therapy-based inhibition of protein kinase Calpha/beta enhances cardiac contractility and attenuates heart failure. Circulation. 2006 Aug 8;114(6):574-82.