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产品名称：MK591
产品别名：喹夫拉朋钠；Quiflapon sodium

生物活性：

Description	Quiflapon sodium (MK591) is a selective and specific 5-Lipoxygenase-activating protein (FLAP) inhibitor.
In Vitro	Quiflapon sodium (MK591) and SB203580 are able to block SEB-induced human PBMC cell proliferation. Quiflapon sodium (MK591) down regulates three genes [for cathepsin L, IL-17 and guanylate binding protein (GBP)-2] that are up regulated by SEB[1]. Quiflapon sodium (MK591) undergoes apoptosis within hours of treatment. Quiflapon sodium (MK591) also induces rapid activation of the stress kinase, c-Jun N-terminal kinase (JNK), which plays an important role in the apoptosis process. Quiflapon sodium (MK591) triggers apoptosis in prostate cancer cells without inhibition of PI3K-Akt, or ERK. Moreover, MK591 and LY294002 (an inhibitor of PI3K) exert synergistic effect in inducing apoptosis in prostate cancer cells[2]. Quiflapon sodium (MK591) influences cAMP response element-binding protein but not Sp1[4].
In Vivo	Hyperoxia groups of mice treated with Quiflapon sodium (MK591) (20, 40 mg/kg) show alveolarization that resembles that of room air controls while untreated hyperoxia groups show definite evidence of aberrant alveolarization but no inflammation[3]. Comparison of the Aβ-immunopositive areas between the placebo and Quiflapon sodium (MK591) (320 mg/kg)-treated group reveals a statistically significant reduction of the amyloid burden in the treated mice. Quiflapon sodium (MK591) also has a significant reduction in brain levels of IL-1β. Mice treated with Quiflapon sodium (MK591) show a statistically significant decrease in the steady-state levels of total CREB and its phosphorylated form at Ser133[4].
Solvent&Solubility	***In Vitro:*** **DMSO : 50 mg/mL** (**82.08 mM;** Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6416 mL	8.2082 mL	16.4163 mL
	5 mM	0.3283 mL	1.6416 mL	3.2833 mL
	10 mM	0.1642 mL	0.8208 mL	1.6416 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: ≥ 2.75 mg/mL (4.51 mM); Clear solution

此方案可获得 ≥ 2.75 mg/mL (4.51 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 27.5 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: ≥ 2.75 mg/mL (4.51 mM); Clear solution 此方案可获得 ≥ 2.75 mg/mL (4.51 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 27.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Mendis C, et al. Effect of 5-lipoxygenase inhibitor MK591 on early molecular and signaling events induced by staphylococcal enterotoxin B in human peripheral blood mononuclear cells. FEBS J. 2008 Jun;275(12):3088-98. [2]. Sarveswaran S, et al. MK591, a leukotriene biosynthesis inhibitor, induces apoptosis in prostate cancer cells: synergistic action with LY294002, an inhibitor of phosphatidylinositol 3'-kinase. Cancer Lett. 2010 May 28;291(2):167-76. [3]. Park MS, et al. 5-Lipoxygenase-activating protein (FLAP) inhibitor MK-0591 prevents aberrant alveolarization in newborn mice exposed to 85% oxygen in a dose- and time-dependent manner. Lung. 2011 Feb;189(1):43-50. [4]. Chu J, et al. Involvement of 5-lipoxygenase activating protein in the amyloidotic phenotype of an Alzheimer's disease mouse model. J Neuroinflammation. 2012 Jun 14;9:127.

实验参考：

Animal Administration	The Tg2576 transgenic mice expressing human APP with the Swedish mutation (K670N/M671L) are used in these studies. They are genotyped by PCR analysis using tail DNA and kept in a pathogen-free environment, on a 12-hour light/dark cycle and have access to food and water ad libitum. All the experiments presented in this paper are performed with female mice. Starting at 7 months of age, mice are randomized to receive MK-591 (40 mg/kg weight) (n=11) or vehicle (n=9) in their chow diet for 8 months until they are 15 months old. Considering that each mouse eats on average 5 g/day of chow diet and the diet is formulated for 320 mg Quiflapon sodium (MK591) per kg diet, the final dose of the active drug is approximately 40 mg/kg weight/day. During the study, mice in both groups gain weight regularly, and no significant difference in weight is detected between the two groups. No macroscopic effect on the overall general health is observed in the animals receiving the active treatment. Post-mortem examination shows no sign of macroscopic pathology in any of the organs considered (spleen, liver, thymus, ileum). [4]
Kinase Assay	LNCaP cells (appr 3×10^5) are plated and treated with inhibitors or solvent vehicle for varying periods of time. Then the cells are lysed in lysis buffer containing 0.2% CHAPS detergent plus protease and phosphatase inhibitors, and the enzymatic activity of Akt is measured by a kit following methods supplied by the manufacturer. [2]
	[1]. Mendis C, et al. Effect of 5-lipoxygenase inhibitor MK591 on early molecular and signaling events induced by staphylococcal enterotoxin B in human peripheral blood mononuclear cells. FEBS J. 2008 Jun;275(12):3088-98.

References	[2]. Sarveswaran S, et al. MK591, a leukotriene biosynthesis inhibitor, induces apoptosis in prostate cancer cells: synergistic action with LY294002, an inhibitor of phosphatidylinositol 3'-kinase. Cancer Lett. 2010 May 28;291(2):167-76. [3]. Park MS, et al. 5-Lipoxygenase-activating protein (FLAP) inhibitor MK-0591 prevents aberrant alveolarization in newborn mice exposed to 85% oxygen in a dose- and time-dependent manner. Lung. 2011 Feb;189(1):43-50. [4]. Chu J, et al. Involvement of 5-lipoxygenase activating protein in the amyloidotic phenotype of an Alzheimer's disease mouse model. J Neuroinflammation. 2012 Jun 14;9:127.