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产品名称：MK-6096
产品别名：Filorexant

生物活性：

Description	Filorexant (MK-6096) is an orally bioavailable potent and selective reversible antagonist of OX1 and OX2 receptor(<3 nM in binding).
IC_{50} & Target	Ki: < 3 nM(Orexin receptor)[1].
In Vitro	In radioligand binding and functional cell based assays Filorexant (MK-6096) demonstrated potent binding and antagonism of both human OX(1)R and OX(2)R (<3 nM in binding, 11 nM in FLIPR), with no significant off-target activities against a panel of >170 receptors and enzymes. Filorexant (MK-6096) occupies 90% of human OX(2)Rs expressed in transgenic rats at a plasma concentration of 142 nM.
In Vivo	Filorexant (MK-6096) dose-dependently reduced locomotor activity and significantly increased sleep in rats (3-30 mg/kg) and dogs (0.25 and 0.5 mg/kg).

Solvent&Solubility

In Vitro:

DMSO : 12.61 mg/mL (29.99 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3782 mL	11.8912 mL	23.7823 mL
	5 mM	0.4756 mL	2.3782 mL	4.7565 mL
	10 mM	0.2378 mL	1.1891 mL	2.3782 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 (5.95 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.95 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 (5.95 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.95 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 (5.95 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.95 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]. Winrow CJ, et al. Pharmacological characterization of MK-6096 - a dual orexin receptor antagonist for insomnia. Neuropharmacology. 2012 Feb;62(2):978-87. [2]. Coleman PJ, et al. Discovery of [(2R,5R)-5-{[(5-fluoropyridin-2-yl)oxy]methyl}-2-methylpiperidin-1-yl][5-methyl-2-(pyrimidin-2-yl)phenyl]methanone (MK-6096): a dual orexin receptor antagonist with potent sleep-promoting properties. ChemMedChem. 2012 Mar 5;7(3):415-24, 337.

实验参考：

Animal Administration	Animal administration[1] The male Sprague Dawley rats (n = 8/study; age: 3-6 months; weight: 450-600 g) were singly housed with water and food ad libitum and a 12 h light: 12 h dark cycle with lights on at 04:00 and off at 16:00. Sleep studies were conducted to evaluate Filorexant (3 and 10 mg/kg, p.o.), DORA-22 (10 mg/kg, p.o.) and almorexant (3 and 30 mg/kg, p.o.), employing a counterbalanced crossover design in which all animals were alternatively treated with drug and vehicle daily for either 3 or 7 consecutive days (for DORA-22 and Filorexant, respectively): 2 baseline days (no dosing), a 2 day vehicle-only run-in, a 3 or 7-day arm of drug or vehicle followed by 3 or 7 days of conditional crossover. Effects of compound treatments relative to vehicle (20% Vitamin E TPGS, p.o.) were evaluated following administration in the active phase).
References	[1]. Winrow CJ, et al. Pharmacological characterization of MK-6096 - a dual orexin receptor antagonist for insomnia. Neuropharmacology. 2012 Feb;62(2):978-87. [2]. Coleman PJ, et al. Discovery of [(2R,5R)-5-{[(5-fluoropyridin-2-yl)oxy]methyl}-2-methylpiperidin-1-yl][5-methyl-2-(pyrimidin-2-yl)phenyl]methanone (MK-6096): a dual orexin receptor antagonist with potent sleep-promoting properties. ChemMedChem. 2012 Mar 5;7(3):415-24, 337.