产品名称：(R)-(+)-WIN 55,212-2 甲磺酸盐
产品别名：WIN 55,212-2 Mesylate

生物活性：

Description	WIN 55,212-2 Mesylate is a potent aminoalkylindole **cannabinoid (CB) receptor** agonist with **K_i**s of 62.3 and 3.3 nM for human recombinant CB1 and CB2 receptors, respectively.
IC_{50} & Target	Ki: 62.3 nM (human recombinant CB1), 3.3 nM (human recombinant CB2)
In Vitro	WIN 55,212-2 is more potent in CHO-CB2 cells than in CHO-CB1 cells by a factor of 6O. WIN 55,212-2 has no effect on arachidonic acid release in CHO-CB2 or control CHO cells. WIN 55,212-2 fails to stimulate any increase in intracellular Ca2+ up to 10 μM[1]. In primary cultures of rat cerebral cortex neurons, WIN 55,212-2 (0.01--100 nM) increases extracellular glutamate levels, displaying a bell-shaped concentration-response curve. The facilitatory effect of WIN 55,212-2 (1 nM) is fully counteracted by SR141716A (10 nM), by the replacement of the normal Krebs Ringer-bicarbonate buffer with a low Ca2+ medium (0.2 mM) and by the IP(3) receptor antagonist xestospongin C (1 μM)[2]. WIN 55,212-2 evokes CGRP release from TG neurons in vitro (EC50=26 μM) in a concentration- and calcium-dependent manner. WIN 55,212-2-2 neither inhibits capsaicin-evokes CGRP release nor does it inhibit forskolin-, isoproteranol- or prostaglandin E2-stimulated cAMP accumulation. WIN 55,212-2 significantly inhibits (EC50=1.7 μM) 50 mm K+-evoked CGRP release by approximately 70%. WIN 55,212-2 inhibition of 50 mm K+-evoked CGRP release is not reversed by antagonists of cannabinoid type 1 (CB1) receptor, but is mimicks in magnitude and potency (EC50=2.7 μM) by its cannabinoid-inactive enantiomer WIN 55,212-2-3[3].
In Vivo	In the prefrontal cortex WIN 55,212-2 (0.1 and 1 mg/kg i.p.) increases dialysate glutamate levels from of the awake rat, while the lower (0.01 mg/kg) and the higher (2 mg/kg) doses are ineffective. Furthermore, the WIN 55,212-2 (0.1 mg/kg)- induced increase of dialysate glutamate levels is counteracted by pretreatment with the selective CB(1) receptor antagonist SR141716A (0.1 mg/kg, i.p.) and by the local perfusion with a low-calcium Ringer solution (Ca2+ 0.2 mM)[2]. WIN 55,212-2 (0.5, 1, 3, 5, 10 and 15 mg/kg, i.p.) does not alter the seizure threshold at low doses, while higher doses of the drug significantly increases the threshold in a dose-dependent manner. The anticonvulsant effect of WIN 55,212-2, which is observed with doses as high as 5 mg/kg, can be observed with doses as low as 0.5 mg/kg in groups pre-treated with 20 mg/kg of pioglitazone[4].

In Vitro:

DMSO : ≥ 34 mg/mL (65.06 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	1.9135 mL	9.5674 mL	19.1347 mL
	5 mM	0.3827 mL	1.9135 mL	3.8269 mL
	10 mM	0.1913 mL	0.9567 mL	1.9135 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:

Solvent&Solubility	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 (4.78 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.78 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 (4.78 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.78 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 (4.78 mM); Precipitated solution; Need ultrasonic 此方案可获得 2.5 mg/mL (4.78 mM) 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]. Felder CC, et al. Comparison of the pharmacology and signal transduction of the human cannabinoid CB1 and CB2 receptors. Mol Pharmacol. 1995 Sep;48(3):443-50. [2]. Ferraro L, et al. The cannabinoid receptor agonist WIN 55,212-2 regulates glutamate transmission in rat cerebral cortex: an in vivo and in vitro study. Cereb Cortex. 2001 Aug;11(8):728-33. [3]. Price TJ, et al. Cannabinoid receptor-independent actions of the aminoalkylindole WIN 55,212-2 on trigeminal sensory neurons. Br J Pharmacol. 2004 May;142(2):257-66. [4]. Payandemehr B, et al. Involvement of PPAR receptors in the anticonvulsant effects of a cannabinoid agonist, WIN 55,212-2. Prog Neuropsychopharmacol Biol Psychiatry. 2015 Mar 3;57:140-5

实验参考：

Animal Administration	In experiment 1, different doses of WIN 55,212-2 (0.5, 1, 3, 5, 10 and 15 mg/kg) are injected 60 min prior to the determination of clonic seizure threshold induced by intravenous administration of PTZ solution. Control animals receive the same volume of the vehicle (1% aqueous solution of DMSO). The doses and time point are chosen on the basis of pilot studies. In experiment 2, in order to confirm the anticonvulsant effects of pioglitazone, different doses (10, 20, 40 and 80 mg/kg) are administered 4 h prior to PTZ in distinct groups of mice. The corresponding control groupreceive the appropriate vehicle (CMC 1%) at the same time point. In experiment 3, The additive anti epileptic effects of WIN 55,212-2 and pioglitazone are examined; mice receive acute administration of pioglitazone (10 or 20 mg/kg) 3 h before WIN 55,212-2 (0.5 or 1 mg/kg) and 4 h before PTZ. [3]
	[1]. Felder CC, et al. Comparison of the pharmacology and signal transduction of the human cannabinoid CB1 and CB2 receptors. Mol Pharmacol. 1995 Sep;48(3):443-50. [2]. Ferraro L, et al. The cannabinoid receptor agonist WIN 55,212-2 regulates glutamate

References	transmission in rat cerebral cortex: an in vivo and in vitro study. Cereb Cortex. 2001 Aug;11(8):728-33. [3]. Price TJ, et al. Cannabinoid receptor-independent actions of the aminoalkylindole WIN 55,212-2 on trigeminal sensory neurons. Br J Pharmacol. 2004 May;142(2):257-66. [4]. Payandemehr B, et al. Involvement of PPAR receptors in the anticonvulsant effects of a cannabinoid agonist, WIN 55,212-2. Prog Neuropsychopharmacol Biol Psychiatry. 2015 Mar 3;57:140-5