

产品名称: **Brexipiprazole**
 产品别名: 依匹哌唑; **OPC-34712**

生物活性:

Description	Brexipiprazole (OPC-34712), an atypical antipsychotic drug, is a partial agonist of human 5-HT1A and dopamine receptor with K _s of 0.12 nM and 0.3 nM, respectively. Brexipiprazole is also a 5-HT2A receptor antagonist with a K _i of 0.47 nM.				
IC ₅₀ & Target	K _i : 0.12 nM (5-HT1A), 0.3 nM (D2L), 0.47 nM (5-HT2A)[1]				
In Vitro	Brexipiprazole (OPC-34712), a novel serotonin-dopamine activity modulator: A role for serotonin 5-HT1A and 5-HT2A receptors. Brexipiprazole also shows potent antagonist activity at human nor adrenergic α1B (K _i =0.17 nM) and α2C receptors (K _i =0.59 nM). Brexipiprazole significantly potentiates nerve growth factor (NGF)-induced neurite outgrowth in PC12 cells, in a concentration dependent manner. Brexipiprazole (1 μM) increases the number of cells with neurites in PC12 cells. Treatment with Brexipiprazole (0.001, 0.01, 0.1 or 1.0 μM) in conjunction with NGF (2.5 ng/mL) increases the number of cells with neurites, in a concentration-dependent manner[1].				
In Vivo	Brexipiprazole (0.01, 0.03, 0.1 mg/kg, p.o.) significantly ameliorates dizocilpine-induced social recognition deficits, without sedation or a reduction of exploratory behavior. In addition, Brexipiprazole alone has no effect on social recognition in untreated controlmice. By contrast, neither Risperidone(0.03 mg/kg, p.o.) nor Olanzapine (0.03 mg/kg, p.o.) alters Dizocilpine induced social recognition deficits. Finally,the effect of Brexipiprazole on Dizocilpine-induced social recognition deficits is antagonized by WAY-100,635. These results suggest that Brexipiprazole can improve Dizocilpine-induced social recognition deficits via 5-HT1A receptor activation in mice[2].				
Solvent&Solubility	In Vitro: DMSO : ≥ 48 mg/mL (110.71 mM) H₂O : < 0.1 mg/mL (insoluble) * "≥" means soluble, but saturation unknown.				
	Preparing Stock Solutions	<div>SolventMassConcentration</div>	1 mg	5 mg	10 mg
		1 mM	2.3064 mL	11.5322 mL	23.0643 mL
		5 mM	0.4613 mL	2.3064 mL	4.6129 mL
		10 mM	0.2306 mL	1.1532 mL	2.3064 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℃, 6 months; -20℃, 1 month。-80℃ 储存时，请在 6 个月内使用，-20℃ 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→ 90% (20% SBE-β-CD in saline)					
Solubility: 2.5 mg/mL (5.77 mM); Suspended solution; Need ultrasonic					
此方案可获得 2.5 mg/mL (5.77 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。					

	<p>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 生理盐水溶液中，混合均匀。</p> <p>2.请依序添加每种溶剂： 10% DMSO \rightarrow90% corn oil</p> <p>Solubility: \geq 2.5 mg/mL (5.77 mM); Clear solution</p> <p>此方案可获得 \geq 2.5 mg/mL (5.77 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。</p> <p>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。</p>
References	<p>[1]. Ishima T, et al. Potentiation of neurite outgrowth by brexpiprazole, a novel serotonin-dopamine activity modulator: a role for serotonin 5-HT1A and 5-HT2A receptors. Eur Neuropsychopharmacol. 2015 Apr;25(4):505-11.</p> <p>[2]. Yoshimi N, et al. Improvement of dizocilpine-induced social recognition deficits in mice by brexpiprazole, a novel serotonin-dopamine activity modulator. Eur Neuropsychopharmacol. 2015 Mar;25(3):356-64.</p>
实验参考：	
Cell Assay	<p>PC12 cells are cultured at 37°C, 5% CO₂ in Dulbecco's modified Eagle's medium (DMEM), supplemented with 5% heat-inactivated fetal bovine serum (FBS), 10% heat-inactivated horse serum, and 1% penicillin-streptomycin. Medium is changed two to three times a week. PC12 cells are plated onto 24- well tissue culture plates coated with poly-D-lysine/laminin. Cells are plated at relatively low density (0.25\times10⁴ cells/cm²) in DMEM medium containing 0.5% FBS, 1% penicillin-streptomycin. Medium containing a minimal level of serum (0.5% FBS) is used. In this study, 2.5 ng/mL of NGF is used to study the potentiating effects of Brexpiprazole on neurite outgrowth. Twenty-four hours after plating, the medium is replaced with DMEM medium containing 0.5% FBS and 1% penicillin-streptomycin with NGF (2.5 ng/mL), with or without Brexpiprazole (0.001, 0.01, 0.1 or 1 μM), WAY-100,635 (5-HT_{1A} receptor antagonist; 10 μM), raclopride (dopamine D₂ receptor antagonist; 10 μM), DOI (5-HT_{2A} receptor agonist; 0.1, 1 or 10 μM), M100,907 (5-HT_{2A} receptor antagonist; 0.1, 1 or 10 μM), xestospingon C (IP₃ receptor antagonist; 1 μM), 2-APB (IP₃ receptor antagonist; 100 μM), fluoxetine (5-HT transporter inhibitor: 1 μM), or paroxetine (5-HT transporter inhibitor: 1 μM). Four days after incubation with NGF (2.5 ng/mL) with or without specified drugs, morphometric analysis is performed on digitized images of live cells taken under phase-contrast illumination, with an inverted microscope linked to a camera. Images of three fields per well are taken, with an average of 100 cells per field. Differentiated cells are counted by visual examination of the field; only cells that had at least one neurite with a length equal to the cell body diameter are counted, and are then expressed as a percentage of the total cells in the field. Counting is performed in blinded manner[1]</p>
Animal Administration	<p>Mice[1]</p> <p>Male C57BL/6NCRSlc mice aged between 4 and 5 weeks old are selected as stranger mice, while animals between 8 and 10 weeks old are used for this study. All mice are housed in groups of five per cage, in a room maintained at 23\pm2°C and 60\pm10% humidity, with a 12/12h light/dark cycle (lights on at 7:00 a.m.). The mice are given free access to food and water. Brexpiprazole is dissolved in 5% (w/v) gum Arabic and administered orally (p.o.), at 10 mL/kg, 1 h prior to sociability testing. The doses of antipsychotic drugs are selected based on doses that did not impact locomotion.</p>
	<p>[1]. Ishima T, et al. Potentiation of neurite outgrowth by brexpiprazole, a novel serotonin-dopamine</p>

References	<p><u>activity modulator: a role for serotonin 5-HT1A and 5-HT2A receptors. Eur Neuropsychopharmacol. 2015 Apr;25(4):505-11.</u></p> <p>[2]. Yoshimi N, et al. Improvement of dizocilpine-induced social recognition deficits in mice by brexpiprazole, a novel serotonin-dopamine activity modulator. Eur Neuropsychopharmacol. 2015 Mar;25(3):356-64.</p>
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源叶生物