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产品名称：甲磺酸溴隐亭
产品别名：Bromocriptine mesylate；CB-154

生物活性：

Description	Bromocriptine mesylate is a potent dopamine D2/D3 receptor agonist, which binds D2 dopamine receptor with pKi of 8.05±0.2.
IC_{50} & Target	pKi: 8.05±0.2 (dopamine D2 receptor)[1]
In Vitro	Bromocriptine stimulates [^{35}S]-GTPγS binding at D2 dopamine receptor expressed in CHO cells with pEC_{50} of 8.15±0.05[1]. Bromocriptine also is a strong inhibitor of brain nitric oxide synthase. The ergot alkaloid Bromocriptine (BKT) is found to act as a strong inhibitor of purified neuronal nitric oxide synthase (NOS) (IC_{50}=10±2 μM) whereas it is poorly active towards inducible macrophage NOS (IC_{50}>100 μM) [2]. Bromocriptine is found to inhibit the activity of at least one human cytochrome P450 enzyme. Bromocriptine is a potent inhibitor of CYP3A4 with a calculated IC_{50} value for the interaction of 1.69 μM[3].
In Vivo	Bromocriptine mesylate (2 mg/kg, i.p.) is administered for 7 days in groups of mice in forced swimming test (FST) and tail suspension test (TST). Bromocriptine group shows significant anti-immobility action as compared to control. When Bromocriptine administered 30 min after the last dose of 7 days MPE treatment and subjected to FST, this dopaminergic agonist produces significant and dose dependent potentiation of anti-immobility action of MPE (200 mg/kg, p.o.) as compared to MPE treatment alone. Bromocriptine treatment group shows a significant reduction of immobility time as compared to control. Bromocriptine administration after 7 days pretreatment with MPE (100 and 200 mg/kg, p.o.) shows significant and dose dependent potentiation of anti-immobility action of MPE as compared to MPE treatment alone[4]. Intracisternal administration of Bromocriptine decreases significantly the static mechanical allodynia (SMA) score compared to that of sham (saline-injected rats) and its effect lasted for 30 min. Intraperitoneal administration of Bromocriptine induces a significant, dose dependent (0.1 mg and 1 mg/kg) decrease in pain scores in CCI-IoN group when compared to sham and its effect lasted for 6 h. The highest dose induces the highest score decrease (P<0.01). Bromocriptine effect lasts for 20 min. Intraperitoneal administration of Bromocriptine induces a significant dose dependent decrease in SMA score in CCI-IoN+6-OHDA lesioned group compared to that of sham. Its effect lasts for 6 h[5].

In Vitro:

DMSO : 75 mg/mL (**99.91 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	1.3321 mL	6.6605 mL	13.3209 mL
	5 mM	0.2664 mL	1.3321 mL	2.6642 mL
	10 mM	0.1332 mL	0.6660 mL	1.3321 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 (sealed storage, away from moisture and light)。-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

Solvent&Solubility	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 (3.33 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.33 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 (3.33 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (3.33 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 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 (3.33 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.33 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]. Gardner B, et al. Agonist action at D2(long) dopamine receptors: ligand binding and functional assays. Br J Pharmacol. 1998 Jul;124(5):978-84. [2]. Renodon A, et al. Bromocriptine is a strong inhibitor of brain nitric oxide synthase: possible consequences for the origin of its therapeutic effects.FEBS Lett. 1997 Apr 7;406(1-2):33-6. [3]. Wynalda MA, et al. Assessment of potential interactions between dopamine receptor agonists and various human cytochrome P450 enzymes using a simple in vitro inhibition screen. Drug Metab Dispos. 1997 Oct;25(10):1211-4. [4]. Rana DG, et al. Dopamine mediated antidepressant effect of Mucuna pruriens seeds in various experimental models of depression. Ayu. 2014 Jan;35(1):90-7. [5]. Dieb W, et al. Nigrostriatal dopaminergic depletion increases static orofacial allodynia. J Headache Pain. 2016;17:11.

实验参考：

	Mice[4] Swiss mice (20-25 g) of either sex (total 150) are used. Bromocriptine mesylate is used as dopamine receptor (D_2) agonist. Haloperidol is diluted in distilled water which is used for a vehicle of injection. Bromocriptine mesylate is dissolved in one drop of glacial acetic acid and made up to volume in distilled water. Imipramine is dissolved in 0.9% normal saline. Haloperidol (0.1 mg/kg, i.p.) and Bromocriptine mesylate (2 mg/kg, i.p.) are administered for 7 days in groups of mice in Forced Swimming Test (FST) and Tail Suspension Test (TST). Imipramine (10 mg/kg, p.o.) as a standard is

Animal Administration	administered in positive control groups for 7 days. Rats[5] Adult male Sprague-Dawley rats (N=112, 275-325 g) are used. Two weeks after the 6-OHDA injection, the animals are briefly (<3 min) anesthetized with 2 % halothane using a mask and received for intracisternal administration Bromocriptine (7 μg/kg dissolved in 5 μL vehicle) or the vehicle alone (5 μL of 0.9 % saline). For i.p. injection we used Bromocriptine (1 mg/kg) and SKF81297 (3 mg/kg dissolved in 0.9 % saline) concentrations. Following a recovery period (<2 min), the rats are placed in the observation field for 40 min period-test by a blind-experimenter.
Kinase Assay	The [^{35}S]-GTPγS binding assay is carried out. Cell membranes (25 ±75 ug) are incubated in Buffer B containing 0.1 mM dithiothreitol (DTT) and 1 uM GDP and drugs in a volume of 0.9 mL for 30 min at 30°C. This preincubation ensures that the agonists tested are at equilibrium when the [^{35}S]-GTPγS (50±150 pM, final concentration) is added (in 100 uL of Buffer B) to initiate the reaction. The assay mixture is incubated for a further 20 min unless otherwise stated. The assays are terminated by rapid filtration and bound radio-activity determined as described for the radio-ligand binding assays above. The total binding of [^{35}S]-GTPγS is less than 20% of that added[1].
References	[1]. Gardner B, et al. Agonist action at D2(long) dopamine receptors: ligand binding and functional assays. Br J Pharmacol. 1998 Jul;124(5):978-84. [2]. Renodon A, et al. Bromocriptine is a strong inhibitor of brain nitric oxide synthase: possible consequences for the origin of its therapeutic effects.FEBS Lett. 1997 Apr 7;406(1-2):33-6. [3]. Wynalda MA, et al. Assessment of potential interactions between dopamine receptor agonists and various human cytochrome P450 enzymes using a simple in vitro inhibition screen. Drug Metab Dispos. 1997 Oct;25(10):1211-4. [4]. Rana DG, et al. Dopamine mediated antidepressant effect of Mucuna pruriens seeds in various experimental models of depression. Ayu. 2014 Jan;35(1):90-7. [5]. Dieb W, et al. Nigrostriatal dopaminergic depletion increases static orofacial allodynia. J Headache Pain. 2016;17:11.