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产品名称：Opicapone
产品别名：BIA 9-1067

生物活性：

Description	Opicapone is a once-daily, potent third-generation catechol-O-methyltransferase (COMT) inhibitor for the treatment of Parkinson's disease and motor fluctuations. Opicapone decreases the ATP content of the cells with IC50 of 98 μM.
IC_{50} & Target	COMT[1]
In Vitro	Opicapone has a prolonged inhibitory effect on peripheral COMT, which extends the bioavailability of levodopa, without inducing toxicity. Opicapone decreases the ATP content of the cells with IC_{50} values of 98 μM. Incubation of human primary hepatocytes for 24 h with increasing concentrations of Tolcapone, entacapone or Opicapone resulted in a concentration-dependent decrease in the mitochondrial membrane potential of the cells, evaluated by the ratio JC-1 aggregates over JC-1 monomer (ratio λ_{ex} 544 λ_{em} 590 over λ_{ex} 485 λ_{em} 538). Opicapone decreases the mitochondrial membrane potential of the cells with IC_{50} of 181 μM[1].
In Vivo	Opicapone inhibits rat peripheral COMT with ED_{50} values below 1.4 mg/kg up to 6 h post-administration. The effect is sustained over the first 8 h and by 24 h COMT had not returned to control values. A single administration of Opicapone resulted in increased and sustained plasma levodopa levels with a concomitant reduction in 3-O-methyldopa from 2 h up to 24 h post-administration, while Tolcapone produced significant effects only at 2 h post-administration. The effects of Opicapone on brain catecholamines after levodopa administration are sustained up to 24 h post-administration. Opicapone is also the least potent compound in decreasing both the mitochondrial membrane potential and the ATP content in human primary hepatocytes after a 24 h incubation period[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 100 mg/mL** (**242.03 mM**; Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4203 mL	12.1016 mL	24.2031 mL
5 mM	0.4841 mL	2.4203 mL	4.8406 mL
10 mM	0.2420 mL	1.2102 mL	2.4203 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 (6.05 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.05 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 (6.05 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (6.05 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。
References	[1]. Bonifácio MJ, et al. Pharmacological profile of Opicapone, a third-generation nitrocatechol catechol-O-methyl transferase inhibitor, in the rat. Br J Pharmacol. 2015 Apr;172(7):1739-52. [2]. Ferreira JJ, et al. Opicapone as an adjunct to levodopa in patients with Parkinson's disease and end-of-dose motor fluctuations: a randomised, double-blind, controlled trial. Lancet Neurol. 2016 Feb;15(2):154-165.

实验参考：

Animal Administration	Rats[1] Male Wistar rats (240) are used. In experiments designed to evaluate the efficacy of the compound at inhibiting COMT, animals are administered Opicapone (0.03, 0.1, 0.3, 0.6, 1, 3 and 10 mg/kg) and are killed at 2 and 6 h post-administration. In experiments designed to evaluate COMT time-activity profile, animals are given Opicapone (3 mg/kg) and are killed at different post-administration periods (15 and 30 min, and 1, 2, 4, 8, 18, 24, and 48 h). In experiments designed to evaluate the effects of the compounds on central catecholamines, animals are given 3 mg/kg Opicapone or Tolcapone and 1 h before being killed, animals are administered levodopa/benserazide (levodopa 12 mg/kg and benserazide 3 mg/kg).
Kinase Assay	ATP content of human primary hepatocytes is determined using the ATP Lite assay system, which is based on the production of light caused by the reaction of ATP with added luciferase and D-luciferin. Twenty-four hours after being seeded, cell cultures are washed with Hank's balanced salt solution (HBSS) and are then incubated with test compounds prepared in culture media without fetal bovine serum (0, 1.56, 3.13, 6.25, 12.5, 25, 50, 100 and 200 μM) for 24 h at 37°C in humidified 5% CO_2-95% air. Positive controls (cells incubated with carbonyl cyanide-p-trifluoromethoxyphenylhydrazone-FCCP, 10 and 50 μM) are run in parallel. After incubation, media are removed from the wells and substituted with 100 μL HBSS plus 50 μL cell lysis solution. Plates are shaken for 5 min at 400 r.p.m. at room temperature. Substrate solution (50 μL) is then added to each well and plates are again shook for 5 min at 400 r.p.m. at room temperature in subdued light. Three standard concentrations of ATP (1, 10 and 100 μM) and blanks are run in parallel in plate wells without cells. Plates are dark adapted for 10 min and luminescence is determined on a MicrobetaTriLux scintillation counter[1].
	[1]. Bonifácio MJ, et al. Pharmacological profile of Opicapone, a third-generation nitrocatechol

References	catechol-O-methyl transferase inhibitor, in the rat. Br J Pharmacol. 2015 Apr;172(7):1739-52. [2]. Ferreira JJ, et al. Opicapone as an adjunct to levodopa in patients with Parkinson's disease and end-of-dose motor fluctuations: a randomised, double-blind, controlled trial. Lancet Neurol. 2016 Feb;15(2):154-165.