

产品名称: **TAK-063**
 产品别名: **Balipodect**

生物活性:				
Description	Balipodect (TAK-063) is a highly potent, selective and orally active PDE10A inhibitor with IC ₅₀ of 0.30 nM; >15000-fold selectivity over other PDEs.			
IC ₅₀ & Target	IC ₅₀ : 0.3 nM (PDE10A)[1].			
In Vitro	<p>Balipodect (TAK-063) has excellent selectivity (>15000-fold selectivity over other PDEs), and favorable pharmacokinetics, including high brain penetration, in mice. Oral administration of Balipodect (TAK-063) to mice elevated striatal 3',5'-cyclic adenosine monophosphate (cAMP) and 3',5'-cyclic guanosine monophosphate (cGMP) levels at 0.3 mg/kg and showed potent suppression of phencyclidine (PCP)-induced hyperlocomotion at a minimum effective dose (MED) of 0.3 mg/kg[1].</p> <p>Balipodect (TAK-063) at 0.3 and 1 mg/kg, p.o., increased cAMP and cGMP levels in the rodent striatum and upregulated phosphorylation levels of key substrates of cAMP-dependent and cGMP-dependent protein kinases. Balipodect (TAK-063) at 0.3 and 1 mg/kg, p.o., strongly suppressed MK-801-induced hyperlocomotion that is often used as a predictive model for antipsychotic-like activity in rodents. Balipodect (TAK-063) did not affect plasma prolactin or glucose levels at doses up to 3 mg/kg, p.o. Balipodect (TAK-063) at 3 mg/kg, p.o., elicited a weak cataleptic response compared with haloperidol and olanzapine[2].</p>			
Solvent&Solubility	<p>In Vitro:</p> <p>DMSO : 25 mg/mL (58.35 mM; Need ultrasonic)</p> <p>H₂O : < 0.1 mg/mL (insoluble)</p>			
	<div>Preparing Stock Solutions</div>	<div>Solvent Mass Concentration</div>	1 mg	5 mg
		1 mM	2.3342 mL	11.6708 mL
		5 mM	0.4668 mL	2.3342 mL
		10 mM	0.2334 mL	1.1671 mL
	<p>*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。</p> <p>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。</p> <p>In Vivo:</p> <p>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：</p> <p>——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</p> <p>1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</p> <p>Solubility: ≥ 2.5 mg/mL (5.84 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.84 mM，饱和度未知) 的澄清溶液。</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 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。</p>			

	<p>2.请依序添加每种溶剂： 10% DMSO →90% corn oil</p> <p>Solubility: ≥ 2.5 mg/mL (5.84 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.84 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]. Kunitomo J, et al. Discovery of <u>1-[2-Fluoro-4-(1H-pyrazol-1-yl)phenyl]-5-methoxy-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one (TAK-063), a Highly Potent, Selective, and Orally Active Phosphodiesterase 10A (PDE10A) Inhibitor</u>. J Med Chem. 2014 Nov 26;57(22):9627-43.</p> <p>[2]. Suzuki K, et al. In Vivo Pharmacological Characterization of TAK-063, a Potent and Selective Phosphodiesterase 10A Inhibitor with Antipsychotic-Like Activity in Rodents. J Pharmacol Exp Ther. 2014 Dec 18. pii: jpet.114.218552.</p>
实验参考：	
Animal Administration	<p>Mice[1]</p> <p>Compound 27h was suspended in 0.5% (w/v) methylcellulose in distilled water. Compound 27h was administered orally (po). PCP hydrochloride (lot no. 010M4010) purchased from Sigma-Aldrich, Inc. (USA) was dissolved in saline and was administered subcutaneously (sc). All compounds were dosed in a volume of 20 mL/kg body weight. Hyperlocomotion was measured using a spontaneous motor analyzer MDC system (BrainScience idea. Co. Ltd., Japan). Mice were placed in locomotor chambers for more than 60 min for habituation. Animals were removed from each chamber and treated with either vehicle or compound 27h and then quickly returned to the chamber. The following doses were used: 0.1, 0.3, and 1.0 mg/kg, po. Sixty minutes after treatment with compound 27h, animals were again removed from the chambers and treated with either vehicle (saline) or PCP (5 mg/kg as a salt, sc) and then quickly transferred to the test chamber. Activity counts were recorded in successive 1 min bins, and the total number counts were determined for the 120 min period after PCP administration.</p>
References	<p>[1]. Kunitomo J, et al. Discovery of <u>1-[2-Fluoro-4-(1H-pyrazol-1-yl)phenyl]-5-methoxy-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one (TAK-063), a Highly Potent, Selective, and Orally Active Phosphodiesterase 10A (PDE10A) Inhibitor</u>. J Med Chem. 2014 Nov 26;57(22):9627-43.</p> <p>[2]. Suzuki K, et al. In Vivo Pharmacological Characterization of TAK-063, a Potent and Selective Phosphodiesterase 10A Inhibitor with Antipsychotic-Like Activity in Rodents. J Pharmacol Exp Ther. 2014 Dec 18. pii: jpet.114.218552.</p>