



上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话: 021-61312973 传真: 021-55068248
网址: www.shyuanye.com
邮箱: shyysw@sina.com

产品名称: **URB602**
产品别名: **URB602**

生物活性:					
Description	URB602 is a selective monoacylglycerol lipase (MGL) inhibitor, which inhibits rat brain MGL with IC ₅₀ of 28±4 μM through a noncompetitive mechanism.				
IC ₅₀ & Target	IC50: 28±4 μM (rat brain MGL)[1]				
In Vitro	Without URB602, the apparent Michaelis constant (K _m) of MGL for 2-AG is 24±1.7 μM and the maximum velocity (V _{max}) is 1814±51 nmol min per mg protein; with URB602, the K _m is 20±0.4 μM and the V _{max} is 541±20 nmol min per mg protein (n=4). When organotypic slice cultures of rat forebrain are incubated with URB602 (100 μM), both baseline and Ca ²⁺ -ionophore-stimulated 2-arachidonoylglycerol (2-AG) concentrations are increased[1]. URB602 is an inhibitor of monoacylglycerol lipase (MGL), a serine hydrolase involved in the biological deactivation of the endocannabinoid 2-arachidonoyl-sn-glycerol (2-AG). URB602 weakly inhibits recombinant MGL (IC ₅₀ =223±63 μM) through a rapid and noncompetitive mechanism[2].				
In Vivo	URB602 at doses of 20 and 40 mg/kg tends to reduce upper GI transit and slow colonic propulsion. When taken together as whole gut transit, URB602 dose dependently inhibits transit (P<0.05) compared with the vehicle control group. The inhibitory action of 40 mg/kg URB602 on whole gut transit is absent in these mice, indicating CB ₁ receptor involvement in the inhibitory action[3]. URB602 decreases the AUC of pain behaviour during the early phase of the formalin test with an ED ₅₀ of 0.06±0.028 μg for JZL184 and 120±51.3 μg for URB602 in adult male Sprague-Dawley rats. Both MGL inhibitors also suppresses pain behaviour during the late phase of formalin pain, with an ED ₅₀ of 0.03±0.011 μg for JZL184 and 66±23.9 μg for URB602[4].				
Solvent&Solubility	<i>In Vitro:</i> DMSO : ≥ 31 mg/mL (104.95 mM) * "≥" means soluble, but saturation unknown.				
	Preparing Stock Solutions	Solvent Concentration Mass	1 mg	5 mg	10 mg
		1 mM	3.3855 mL	16.9273 mL	33.8547 mL
		5 mM	0.6771 mL	3.3855 mL	6.7709 mL
		10 mM	0.3385 mL	1.6927 mL	3.3855 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。					
	[1]. Hohmann AG, et al. An endocannabinoid mechanism for stress-induced analgesia. Nature. 2005 Jun 23;435(7045):1108-12. [2]. King AR, et al. URB602 inhibits monoacylglycerol lipase and selectively blocks 2-arachidonoylglycerol degradation in intact brain slices. Chem Biol. 2007 Dec;14(12):1357-65.				



上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话: 021-61312973 传真: 021-55068248
网址: www.shyuanye.com
邮箱: shyysw@sina.com

References	[3]. Duncan M, et al. Distribution and function of monoacylglycerol lipase in the gastrointestinal tract. <i>Am J Physiol Gastrointest Liver Physiol</i>. 2008 Dec;295(6):G1255-65. [4]. Guindon J, et al. Peripheral antinociceptive effects of inhibitors of monoacylglycerol lipase in a rat model of inflammatory pain. <i>Br J Pharmacol</i>. 2011 Aug;163(7):1464-78.
实验参考:	
Animal Administration	Mice[3] Male C57BL/6 mice (5-6 wk; 20-26 g) or female CB1^{-/-} mice (8 wk; 18-22 g) on a C57BL/6 background are used. After an overnight fasting period (water ad libitum), a marker is administered orally to assess upper GI transit, as described in detail by others. At 30 min after intraperitoneal (ip) administration of URB602 (20 or 40 mg/kg) or vehicle (10% DMSO/Tween 80 in saline), an oral gavage of 200 μL of an Evans blue marker (5% Evans blue, 5% gum arabic) is administered. After 15 min animals are killed by cervical dislocation and the intestine from the region of the pyloric sphincter to the ileocecal junction is immediately removed. The distance traveled by the marker is measured in centimeters and expressed as a percentage of the total length of the small intestine. Rats[4] Three hundred and seven adult male Sprague-Dawley rats weighing 275-350 g, at the time of testing, are used. In a first study, the dose-response curves for JZL184 and URB602 are determined using the AUC of Phase 1 or Phase 2 pain behaviour. In a second study, the antinociceptive effects of JZL184 (300 μg) and URB602 (600 μg) are evaluated following injection in the paw, ipsilateral or contralateral to formalin, to exclude the possibility that systemic leakage contributed to the pattern of results obtained. In a third study, antinociceptive effects of ED₅₀doses of JZL184 (0.03 μg i.paw) or URB602 (66 μg i.paw), in combination with 2-AG (ED₅₀ dose of 1 μg i.paw), are quantified to evaluate the presence of additive or synergic effects of these drugs. In a fourth study, antinociceptive effects of JZL184 (at 10 μg i.paw, an analgesic dose) are studied in the presence or absence of either AM251 or AM630 to determine whether these effects are mediated through CB₁ and/or CB₂ receptors. The CB₁ receptor antagonist AM251 exhibits 306-fold selectivity for CB₁ over CB₂ receptors, whereas the CB₂ receptor antagonist AM630 exhibits 70-165-fold selectivity for CB₂ over CB₁ receptors. The doses employed (AM251 at 80 μg i.paw and AM630 at 25 μg i.paw) are those which block peripheral antinociceptive effects of URB602 in Wistar rats. For the first study (n=4-6 per group for URB602 and n=6-8 per group for JZL184) and for all the other behavioural studies (n=6 per group), drugs, administered either alone or in combination, are dissolved in the same total volume (50 μL) and injected into the right hind paw. Preliminary experiments (n=8 per group; data not shown) confirmed that formalin-induced pain behaviour did not change following intra-paw administration of either vehicle (PEG 300: Tween 80 in a 4:1 ratio or DMSO: ethanol: cremophor: 0.9% saline in a 1:1:1:17 ratio).
Kinase Assay	Samples containing either URB602 (300 μM), MGL (1.4 pM), or both URB602 and MGL are incubated at 37°C for 30 min in assay buffer. At various time points, the reaction is stopped with an equal volume of ice-cold methanol and directly analyzed in positive ionization mode by LC/MS. A SB-CN column (150$\times$2.1 mm i.d., 5 μm) eluted is used with a linear gradient of methanol in water containing 0.25% acetic acid and 5 mM ammonium acetate (from 60% to 100% of methanol in 8 min) at a flow rate of 0.5 mL/min with column temperature at 50°C. Capillary voltage is set at 4 kV



上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话: 021-61312973 传真: 021-55068248
网址: www.shyuanye.com
邮箱: shyysw@sina.com

	and fragmentor voltage is 100V. Nebulizer pressure is set at 60 psi. N ₂ is used as drying gas at a flow rate of 13 liters/min and a temperature of 350°C. ESI is in the positive mode and a full scan spectrum is acquired from m/z 100 to 600. Extracted ion chromatograms are used to quantify URB602 ([M+H] ⁺ , m/z 296)[2].
References	[1]. Hohmann AG, et al. An endocannabinoid mechanism for stress-induced analgesia. Nature. 2005 Jun 23;435(7045):1108-12. [2]. King AR, et al. URB602 inhibits monoacylglycerol lipase and selectively blocks 2-arachidonoylglycerol degradation in intact brain slices. Chem Biol. 2007 Dec;14(12):1357-65. [3]. Duncan M, et al. Distribution and function of monoacylglycerol lipase in the gastrointestinal tract. Am J Physiol Gastrointest Liver Physiol. 2008 Dec;295(6):G1255-65. [4]. Guindon J, et al. Peripheral antinociceptive effects of inhibitors of monoacylglycerol lipase in a rat model of inflammatory pain. Br J Pharmacol. 2011 Aug;163(7):1464-78.