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产品名称: **YM758**
CAS 号: **312752-85-5**
货号: **S89663**

生物活性:						
Description		YM758 is a "funny" If current channel (If channel) inhibitor.				
IC50 & Target		If channel[1]				
In Vitro		The inhibitory effect of YM758 on [3H]MPP uptake via human/rat organic cation transporters (hOCT1/rOCT1) is investigated. YM758 inhibits rOCT1- and hOCT1-mediated [3H]MPP uptake in a concentration-dependent manner with IC50 values of 23.8 and 40.5 μM, respectively. The IC50 value of YM758 for [14C]Metformin uptake via rOCT1 may be estimated below 10 μM in the same way, whereas that is much smaller than that for [3H]MPP uptake. In addition, the inhibitory effect of YM758 on [3H]E217βG uptake via OATP1B1 and OATP1B3 is investigated. YM758 inhibits OATP1B1-mediated [3H]E217βG uptake in a concentration-dependent manner with a IC50 value of 13.0 μM. YM758 has no inhibitory effect on OATP1B3-mediated [3H]E217βG uptake[1].				
In Vivo		After a single intravenous administration of 0.03, 0.1, and 0.3 mg/kg to tachycardia-induced beagles, YM758 plasma concentrations rapidly decrease with t1/2 values of 1.62, 4.93, and 1.63 h, respectively. At the corresponding doses, the CLtot values amount to 1.71, 1.69, and 1.48 L/h/kg, and Vdss values are 3.19, 5.78, and 2.94 L/kg, respectively. Because the plasma concentration 24 h after administration is quantified only in the 0.1 mg/kg dosing group, the larger values of t1/2 and Vdss are obtained compared with those in other dosing groups. The PK profile of YM758 in tachycardia-induced dogs appears to be linear within the dose range of 0.03 to 0.3 mg/kg. The CLtot of YM758 in the blood basis (CLb,dog) is estimated to be 1.47 to 1.69 L/h/kg[2]. The radioactivity in the rat eyeballs after dosing 14C-YM758 is extracted with a mixture of 2 mol/L hydrochloric acid and Methanol (5:95, v/v); the radioactivity recovery is 97.1% at 4 h and 67.1% at 24 h. The HPLC recovery of radioactivity from the extracted samples is 90.6 and 100.6% at 4 and 24 h, respectively. In the eyeball at 4 h after administration, YM758 (the unchanged drug) is the main compound detected (66.7%), and the metabolites YM-252124 (14.5%), YM-394111 (2.4%), and YM-234903 (1.8%) are also observed[3].				
Solvent&Solubility		细胞实验: DMSO 中的溶解度 : 100 mg/mL (212.97 mM); 超声助溶 (<60°C); 吸湿的 DMSO 对产品的溶解度有显著影响, 请使用新开封的 DMSO)				
		Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
			1 mM	2.1297 mL	10.6485 mL	21.2970 mL
			5 mM	0.4259 mL	2.1297 mL	4.2594 mL
			10 mM	0.2130 mL	1.0648 mL	2.1297 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。						
参考文献		[1]. Umehara K, et al. Hepatic uptake and excretion of (-)-N-{2-[(R)-3-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline-2-carbonyl)piperidino]ethyl}-4-fluorobenzamide (YM758), a novel if channel inhibitor, in rats and humans. Drug Metab Dispos. 2008 Jun;36(6):1030-8. [2]. Umehara K, et al. Relationship between exposure of				



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	(-)-N-{2-[(R)-3-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline-2-carbonyl)piperidino]ethyl}-4-fluorobenzamide (YM758), a "funny" if current channel inhibitor, and heart rate reduction in tachycardia-induced beagle dogs. Drug Metab Dispos. 2009 Jul;37(7):1427-33. [3]. Umehara K, et al. Investigation of long-term retention of unchanged (-)-N-{2-[(R)-3-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline-2-carbonyl)piperidino]ethyl}-4-fluorobenzamide, a novel "funny" If current channel inhibitor, and its metabolites in the eyeball and thoracic aorta of rats. Drug Metab Dispos. 2009 Nov;37(11):2137-44.
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完整储备液配制表:

* 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。

可选溶剂	质量 溶剂体积 浓度	1 mg	5 mg	10 mg	25 mg
DMSO	1 mM	3.0926 mL	15.4631 mL	30.9262 mL	77.3156 mL
	1 mM	2.1297 mL	10.6485 mL	21.2970 mL	53.2425 mL
	5 mM	0.4259 mL	2.1297 mL	4.2594 mL	10.6485 mL
	10 mM	0.2130 mL	1.0648 mL	2.1297 mL	5.3242 mL
	15 mM	0.1420 mL	0.7099 mL	1.4198 mL	3.5495 mL
	20 mM	0.1065 mL	0.5324 mL	1.0648 mL	2.6621 mL
	25 mM	0.0852 mL	0.4259 mL	0.8519 mL	2.1297 mL
	30 mM	0.0710 mL	0.3549 mL	0.7099 mL	1.7747 mL
	40 mM	0.0532 mL	0.2662 mL	0.5324 mL	1.3311 mL
	50 mM	0.0426 mL	0.2130 mL	0.4259 mL	1.0648 mL
	60 mM	0.0355 mL	0.1775 mL	0.3549 mL	0.8874 mL
	80 mM	0.0266 mL	0.1331 mL	0.2662 mL	0.6655 mL
	100 mM	0.0213 mL	0.1065 mL	0.2130 mL	0.5324 mL