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产品名称：VU 0357017 Hydrochloride
产品别名：CID-25010775

生物活性：

Description

VU0357017 hydrochloride is a highly selective M1 agonists that appear to act at an allosteric site to activate the receptor (EC50 = 477 ± 172 nM; pEC50 = 6.37 ± 0.15). IC50 value: 477 ± 172 nM (EC50) [1] Target: M1 in vitro: VU0357017 is a M1-selective agonists that appear to activate M1 through actions at an allosteric site. Ki values of VU0357017 derived from competition binding experiment is 9.91(rM1), 21.4 (rM2), 55.3 (rM3), 35 (rM4), and 50 (rM5), respectively. [1] VU0357017 is a potent and efficacious M1 agonist, selective versus M2 M5 family members and allosteric agonist. VU0357017 is a highly selective M1 agonist suggests that these compounds are unlikely to act at the highly conserved orthosteric site on M1 and are more likely to act as allosteric agonists. [2] VU0357017 has robust effects on M1-activation of calcium mobilization and ERK1/2 phosphorylation but have little effect on β-arrestin recruitment. VU0357017 induces calcium release and ERK phosphorylation but is without effects on β-arrestin recruitment. VU0357017 significantly enhances threshold Θ-burst LTP and VU0364572 induces LTD at the Schaffer collateral-CA1 synapse of rodent hippocampal slices. [3] in vivo: VU0357017 has robust efficacy in improving hippocampal-dependent learning in rats. VU0357017 enhances performance in Morris water maze and contextual fear conditioning in rats. [3]

Solvent&Solubility

In Vitro:

DMSO : 25 mg/mL (67.59 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7035 mL	13.5175 mL	27.0351 mL
5 mM	0.5407 mL	2.7035 mL	5.4070 mL
10 mM	0.2704 mL	1.3518 mL	2.7035 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 (6.76 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.76 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 (6.76 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.76 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 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 (6.76 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.76 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]. Digby GJ, et al. Chemical modification of the M(1) agonist VU0364572 reveals molecular switches in pharmacology and a bitopic binding mode. ACS Chem Neurosci. 2012 Dec 19;3(12):1025-36. [2]. Lebois EP, et al. Discovery and characterization of novel subtype-selective allosteric agonists for the investigation of M(1) receptor function in the central nervous system. ACS Chem Neurosci. 2010;1(2):104-121. [3]. Digby GJ, et al. Novel allosteric agonists of M1 muscarinic acetylcholine receptors induce brain region-specific responses that correspond with behavioral effects in animal models. J Neurosci. 2012 Jun 20;32(25):8532-44. [4]. Sheffler DJ, et al. Further exploration of M? allosteric agonists: subtle structural changes abolish M? allosteric agonism and result in pan-mAChR orthosteric antagonism. Bioorg Med Chem Lett. 2013 Jan 1;23(1):223-7.