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产品名称：3-(1H-tetrazol-5-yl)-1,4,5,6-tetrahydrocyclopenta[c]pyrazole
产品别名：MK-0354

生物活性：

Description

MK-0354 is a partial agonist of GPR109a receptor, for hGPR109a/ mGPR109a with EC50 of 1.65/1.08 μM, showed no activation of GPR109b. IC50 value: 1.65 μM (EC50, for hGPR109a), 1.08 μM (EC50, for mGPR109a) [1] Target: GPR109a in vitro: MK-0354 demonstrated clear and statistically significant partial agonism in the cAMP assays for both the mouse and human receptors with efficacy approximately 60-70% of that of either nicotinic acid or β-hydroxy butyrate, a putative physiologically relevant ligand for hGPR109a, in the same assay platform. In addition, MK-0354 showed no activation of GPR109b in the cAMP assay at any concentration up to 100 μM. Following these interesting observations, we then prepared a number of other 5,5-fused pyrazoles analogous to those that showed receptor activity in our earlier studies. MK-0354 appeared to be somewhat unique among the members of the pyrazole tetrazole series in having reasonable receptor activity.[1] in vivo: MK-0354 retained the plasma free fatty acid lowering effects in mice associated with GPR109a agonism, but did not induce vasodilation at the maximum feasible dose. Moreover, preadministration of MK-0354 blocked the flushing effect induced by nicotinic acid but not that induced by PGD2. This profile made MK-0354 a suitable candidate for further study for the treatment of dyslipidemia.[1] MK-0354 is a GPR109A partial agonist that activates the antilipolytic pathway in adipocytes. The single-dose and multiple-dose pharmacokinetics and pharmacodynamics, as well as tolerability, of MK-0354 were examined in two Phase I studies conducted in healthy male volunteers. The lipid efficacy of MK-0354 was assessed in a Phase II study conducted in male and female patients with dyslipidemia.[2]

Solvent&Solubility

In Vitro:

DMSO : ≥ 36 mg/mL (204.34 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	5.6760 mL	28.3801 mL	56.7601 mL
5 mM	1.1352 mL	5.6760 mL	11.3520 mL
10 mM	0.5676 mL	2.8380 mL	5.6760 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 (14.19 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (14.19 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 (14.19 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (14.19 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。
References	[1]. Semple G, et al. 3-(1H-Tetrazol-5-yl)-1,4,5,6-tetrahydro-cyclopentapyrazole (MK-0354): A Partial Agonist of the Nicotinic Acid Receptor, G-Protein Coupled Receptor 109a, with Antilipolytic but No Vasodilatory Activity in Mice. J. Med. Chem., 2008, 51 (16) [2]. Lai E1, et al. Effects of a niacin receptor partial agonist, MK-0354, on plasma free fatty acids, lipids, and cutaneous flushing in humans. J Clin Lipidol. 2008 Oct;2(5):375-383.