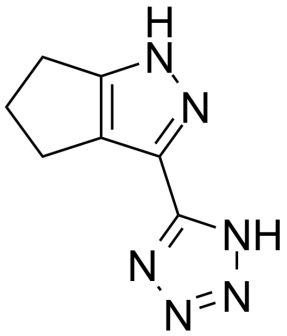
MK-0354

Cat. No.:	HY-13008
CAS No.:	851776-28-8
Molecular Formula:	$C_7H_8N_6$
Molecular Weight:	176.18
Target:	GPR109A
Pathway:	GPCR/G Protein
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 36 mg/mL (204.34 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / 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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (14.19 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (14.19 mM); Clear solution

BIOLOGICAL ACTIVITY

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: GPR109ain 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]

CUSTOMER VALIDATION

- Nat Commun. 2023 Mar 27;14(1):1710.

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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.

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