

Product Data Sheet

Product Name: MK-0354

Cat. No.: GC32464

Chemical Properties

Cas. No. 851776-28-8

SMILES C12=C(CCC2)C(C3=NN=NN3)=NN1

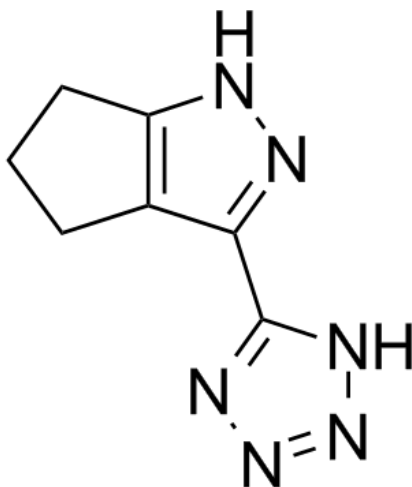
Formula C7H8N6 M.Wt 176.18

Solubility DMSO : ≥ 36 mg/mL (204.34 mM) Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Background

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

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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]

[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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