

Product Data Sheet

Product Name: MK-3903

Cat. No.: GC31361

Chemical Properties

Cas. No. 1219737-12-8

SMILES C1C=CC2=C(NC(OC3=CC=C(C)C(C(O)=O)=C3)=N2)C=C1C(C=C4)=CC=C4C5=CC=CC=C5

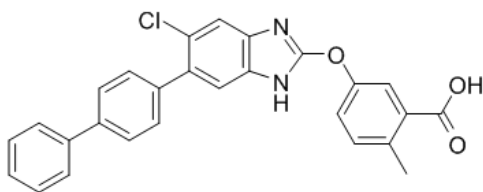
Formula $C_{27}H_{19}ClN_2O_3$ M.Wt 454.9

Solubility DMSO : 75 mg/mL (164.87 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



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

**Kinase
experiment:**

The enzymatic reaction is performed. Briefly, the AMPK complex of interest is appropriately diluted in AMPK reaction buffer and incubated at room temperature for 30 min to yield pAMPK. Then, MK-3903 (compound 42) and pAMPK are pre-incubated by adding appropriately diluted MK-3903 in DMSO (1.2 μ L total) to the reaction buffer containing pAMPK (15 μ L per well), the plate is vortexed briefly and then incubated at room temperature for 30 min. The plate is sealed and incubated at room temperature for 60 min, at which time the reaction is stopped by the addition of quench buffer. EC₅₀s and %activation parameters are calculated from %product vs. activator concentration plots[1].

**Animal
experiment:**

DIO mice at 17 weeks of age are used in this study. Mice are conditioned to dosing with vehicle (5% Tween 80, 0.25% methylcellulose, 0.02% SDS) at 5 mL/kg BID for 5 days. At that time, mice are bled, glucose and insulin measured and the animals sorted into treatment groups based on glucose, insulin and body weight. Each group of animals receives administration of MK-3903 (compound 42) in vehicle at 3 mg/kg, 10 mg/kg, 30 mg/kg, or vehicle alone for 12-day BID. Another group of mice receiving MK-3903 with vehicle at 30 mg/kg for 12-day QD is included as well. Food intake and body weight are measured daily[1].

References:

[1]. Lan P, Romero FA, et al. Hit-to-Lead Optimization and Discovery of 5-((5-([1,1'-Biphenyl]-4-yl)-6-chloro-1H-benzo[d]imidazol-2-yl)oxy)-2-methylbenzoic Acid (MK-3903): A Novel Class of Benzimidazole-Based Activators of AMP-Activated Protein Kinase. J Med Chem. 2017 Nov 9;60(21):9040-9052.

Background

MK-3903 is a potent and selective AMP-activated protein kinase (AMPK) activator with an EC₅₀ of 8 nM.

MK-3903 (compound 42) is a potent and selective AMP-activated protein kinase (AMPK) activator

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

with an EC₅₀ of 8 nM. MK-3903 activates 10 of the 12 phosphorylated AMPK (pAMPK) complexes with EC₅₀ values in the range of 8 to 40 nM and maximal activation >50%. MK-3903 partially activates pAMPK5 (36% max) and it does not activate pAMPK6. MK-3903 demonstrates low permeability ($P_{app}=6\times 10^{-6}$ cm/s) in LLC-PK1 cells⁴² and is a substrate of human liver uptake transporters OATP1B1 and OATP1B3 (organic anion transporter proteins). Results show that MK-3903 binds moderately to the prostanoid DP2 (CRTH2) receptor (binding IC₅₀=1.8 μ M) but not in the presence of 10% human serum (binding IC₅₀>86 μ M)[1].

The pharmacokinetics of MK-3903 (compound 42) in C57BL/6 mice, Sprague to Dawley rats, and beagle dogs are characterized by moderate systemic plasma clearance (5.0 to 13 mL/min/kg), a volume of distribution at steady state of 0.6 to 1.1 L/kg, and a terminal half-life of ~2h. Acute oral administration of MK-3903 (3, 10, and 30 mg/kg) to high-fructose fed db/+ mice results in significant inhibition of hepatic fatty acid synthesis (FAS) for all three doses[1].

[1]. Lan P, Romero FA, et al. Hit-to-Lead Optimization and Discovery of 5-((5-([1,1'-Biphenyl]-4-yl)-6-chloro-1H-benzo[d]imidazol-2-yl)oxy)-2-methylbenzoic Acid (MK-3903): A Novel Class of Benzimidazole-Based Activators of AMP-Activated Protein Kinase. J Med Chem. 2017 Nov 9;60(21):9040-9052.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA