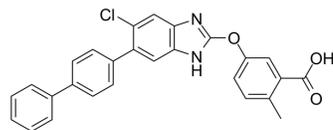


MK-3903

| | | | |
|--------------------|---|-------|---------|
| Cat. No.: | HY-107988 | | |
| CAS No.: | 1219737-12-8 | | |
| Molecular Formula: | C ₂₇ H ₁₉ ClN ₂ O ₃ | | |
| Molecular Weight: | 454.9 | | |
| Target: | AMPK | | |
| Pathway: | Epigenetics; PI3K/Akt/mTOR | | |
| 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 : ≥ 100 mg/mL (219.83 mM)
 * "≥" means soluble, but saturation unknown.

| Concentration | Mass | | |
|---------------|-----------|------------|------------|
| | 1 mg | 5 mg | 10 mg |
| 1 mM | 2.1983 mL | 10.9914 mL | 21.9829 mL |
| 5 mM | 0.4397 mL | 2.1983 mL | 4.3966 mL |
| 10 mM | 0.2198 mL | 1.0991 mL | 2.1983 mL |

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (5.50 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (5.50 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

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

IC₅₀ & Target

AMPK
 8 nM (EC₅₀)

In Vitro

MK-3903 (compound 42) is a potent and selective AMP-activated protein kinase (AMPK) activator 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}=6×10⁻⁶ 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 $IC_{50}=1.8 \mu M$) but not in the presence of 10% human serum (binding $IC_{50}>86 \mu M$)^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay ^[1]

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 μL total) to the reaction buffer containing pAMPK (15 μL 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. EC_{50} s and %activation parameters are calculated from %product vs. activator concentration plots^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^[1]

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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Drug Des Dev Ther. 2020 Aug 19;14:3385-3391.
- Research Square Print. 2023 Feb 3.

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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 C

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

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