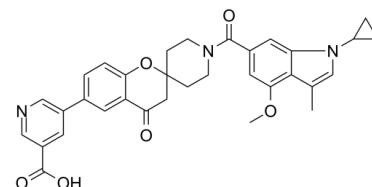


## Data Sheet

Product Name:	MK-4074
Cat. No.:	CS-0029249
CAS No.:	1039758-22-9
Molecular Formula:	C33H31N3O6
Molecular Weight:	565.62
Target:	Acetyl-CoA Carboxylase
Pathway:	Metabolic Enzyme/Protease
Solubility:	DMSO : 83.3 mg/mL (147.27 mM; Need ultrasonic)



### BIOLOGICAL ACTIVITY:

MK-4074 is a liver-specific inhibitor of **acetyl-CoA carboxylase** ACC1 and ACC2 with  $IC_{50}$  values of approximately 3 nM.  $IC_{50}$  & Target:  $IC_{50}$ : 3 nM (Acetyl-CoA Carboxylase)<sup>[1]</sup> **In Vitro**: MK-4074 strongly inhibits both ACC1 and ACC2 with  $IC_{50}$  values of approximately 3 nM. MK-4074 is highly liver specific because it is a substrate of organic anion transport protein (OATP) transporters that are present only in hepatocytes, and excretion of MK-4074 from hepatocytes into bile is dependent on the MRP2 efflux transporter<sup>[1]</sup>. **In Vivo**: In male KKAY mice, a mouse model of obesity, type 2 diabetes, and fatty liver, a single oral dose of MK-4074 (0.3-3 mg/kg) significantly decreases DNL in a dose-dependent manner with an  $ID_{50}$  value of 0.9 mg/kg 1 hr post-administration. In a time course study, MK-4074 orally at 30 mg/kg reduces hepatic DNL by 83%, 70%, and 51% at 4, 8, and 12 hr post-dose, respectively. Single oral doses of MK-4074 at 30 and 100 mg/kg significantly increases plasma total ketones, a surrogate biomarker for hepatic FAO, by 1.5-fold to 3-fold for up to 8 hr<sup>[1]</sup>.

### PROTOCOL (Extracted from published papers and Only for reference)

**Kinase Assay:** <sup>[1]</sup>Recombinant ACC protein is purified from FM3A or Sf9 cells expressing recombinant ACC by chelating chromatography or from liver by Softlink avidin resin chromatography. Purified ACC protein is incubated with **MK-4074** in assay buffer containing 5 mM ATP, 250 mM acetyl-CoA, 4.1 mM NaHCO<sub>3</sub>, 0.086 mM NaH<sub>14</sub>CO<sub>3</sub>, 20 mM potassium citrate, 20 mM MgCl<sub>2</sub>, 2 mM DTT, 0.5 mg/mL BSA and 50 mM HEPES-Na (pH 7.5) for 40 min at 37°C<sup>[1]</sup>. **Cell Assay:** <sup>[1]</sup>For cellular assays of DNL and FAO, cells are pre-incubated with **MK-4074** for 1 hr. Then the cells are incubated for additional 1-3 hr with either 65-260 mM <sup>14</sup>C-labeled acetate or 0.018 mM <sup>3</sup>H-labeled palmitate for DNL or FAO assay, respectively. After incubation, intracellular <sup>14</sup>C-labeled lipids and released <sup>3</sup>H-labeled fatty acids are extracted and measured for DNL and FAO, respectively<sup>[1]</sup>. **Animal Administration:** MK-4074 is prepared in water<sup>[1]</sup>.<sup>[1]</sup>Mice<sup>[1]</sup>

Studies are performed in **male KKAY mice or C57BL/6J mice**. KKAY mice are fed a chow diet while C57BL/6J mice are fed a high-fat diet (45% fat) for 3 weeks prior to study. Mice are treated for 7 days with vehicle (distilled water, 0.2 mL/mouse) before MK-4074 administration to acclimate mice to oral dosing. Animals are drug naive at the time of study. Mice are housed individually. Male KKAY mice (n=10-11/group) are administered a single oral dose of **MK-4074 (0.3 to 3 mg/kg)** prior to liver slice studies. Male KKAY mice (n=5/group) are administered a single oral dose of **MK-4074 (3 to 30 mg/kg)** prior to measurement of liver DNL rates. Male KKAY mice (n=8/group) are administered a single oral dose of **MK-4074 (10 to 100 mg/kg)** and plasma ketone bodies are measured at the indicated times. Male C57BL/6J mice (n=5, veh; n=10, MK-4074) are fed chow or a high-fat/high-sucrose (HF/HS) diet for 7 weeks and vehicle or MK-4074 is administered orally (10 or 30 mg/kg/day) for 4 weeks prior to study<sup>[1]</sup>.

### References:

[1]. Kim CW, et al. Acetyl CoA Carboxylase Inhibition Reduces Hepatic Steatosis but Elevates Plasma Triglycerides in Mice and Humans: A Bedside to Bench Investigation. Cell Metab. 2017 Aug 1;26(2):394-406.e6.

**CAIndexNames:**

3-Pyridinecarboxylic acid, 5-[1'-[(1-cyclopropyl-4-methoxy-3-methyl-1H-indol-6-yl)carbonyl]-3,4-dihydro-4-oxospiro[2H-1-benzopyran-2,4'-piperidin]-6-yl]-

**SMILES:**

O=C1CC2(CCN(C(C3=CC(OC)=C4C(N(C5CC5)C=C4C)=C3)=O)CC2)OC6=CC=C(C7=CN=CC(C(O)=O)=C7)C=C16

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

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: [sales@ChemScene.com](mailto:sales@ChemScene.com)

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA