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# 产品名称：CP-640186
# CAS 号：591778-68-6
# 产品货号：S88247

## 生物活性：

**Description**

CP-640186 是一种具有口服活性的、可透过细胞的乙酰-CoA 羧化酶 (ACC) 抑制剂，其对大鼠肝脏 ACC1 和大鼠骨骼肌 ACC2 的 IC50s 分别为 53 nM 和 61 nM。乙酰-CoA 羧化酶 (ACC) 是脂肪酸代谢的一个关键酶，能够合成丙二酰-CoA。CP-640186 还可以刺激肌肉脂肪酸的氧化。

**IC50 & Target**

IC50: 53 nM (rat liver ACC1) and 61 nM (rat skeletal muscle ACC2)[1].

**Cellular Effect**

| Cell Line | Type | Value | Description |
|---|---|---|---|
| HepG2 | $IC_{50}$ | 0.84 μM | Inhibition of fatty acid synthesis in human HepG2 cells after 48 hrs |

**In Vitro**

CP-640186 (20 μM; 48 h) treatment can inhibit H460 cell growth[3].

CP-640186 (0.1 nM-100 μM; 2 h) treatment increases fatty acid metabolism in a concentration-dependent manner in C2C12 cells and muscle strips[1].

CP-640186 (0.62-1.8 μM; 2 h) treatment inhibits fatty acid synthesis and TG synthesis in HepG2 cells[1]。

Cell Proliferation Assay[3]

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| Cell Line: | Human fibroblasts and H460 cells |
| Concentration: | 20 μM |
| Incubation Time: | 48 hours |
| Result: | Led to a ~ 30% decrease in cell number compared to vehicle-treated controls. |

Cell Viability Assay[1]

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|---|---|
| Cell Line: | C2C12 cells and muscle strips |
| Concentration: | 0.1 nM-100 μM |
| Incubation Time: | 2 hours |
| Result: | Stimulated palmitate acid oxidation with an $EC_{50}$ of 57 nM and a maximal stimulation of 280% in C2C12 cells.<br>Stimulated palmitate acid oxidation with an $EC_{50}$ of 1.3 μM and a maximal stimulation of 240% in isolated rat epitrochlearis muscle. |

Cell Viability Assay[1]

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| Cell Line: | HepG2 cells |
| Concentration: | 0.62-1.8 μM |
| Incubation Time: | 6 hours |
| Result: | Inhibited fatty acid synthesis and TG synthesis in HepG2 cells with $EC_{50}$s of 0.62 μM and 1.8 μM, respecticely. |

**In Vivo**

CP-640186 (oral gavage; 4.6-21 mg/kg; once) demonstrates acute efficacy[1].

CP-640186 (intravenous injection and oral gavage; Intravenous dose, 5 mg/kg; oral dose, 10 mg/kg; once) shows lowe drug exposure in the rat than the ob/ob mouse at equal doses[1].

CP-640186 (oral gavage; 100 mg/kg; once) treatment shows a complete shift from carbohydrate utilization to fatty acid utilization as a source of energy at high exposure level[1]。

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| **Animal Model:** | Male ob/ob mice[1] |
| **Dosage:** | 4.6-21 mg/kg |
| **Administration:** | Oral gavage; 4.6-21 mg/kg; once |

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|---|---|---|
| | **Result:** | Demonstrated acute efficacy for up to 8 h after oral administration, exhibiting $ED_{50}$ values of 4.6, 9.7, and 21 mg/kg, at 1, 4, and 8 h, respectively, after treatment. |
| | **Animal Model:** | Male Sprague-Dawley rats[1] |
| | **Dosage:** | Intravenous dose, 5 mg/kg; oral dose, 10 mg/kg |
| | **Administration:** | Intravenous injection and oral gavage; Intravenous dose, 5 mg/kg; oral dose, 10 mg/kg; once |
| | **Result:** | Showed a plasma half-life of 1.5 h, a bioavailability of 39%, a $Cl_p$ of 65 ml/min/kg, a $V_{dss}$ of 5 liters/kg, an oral $T_{max}$ of 1.0 h, an oral $C_{max}$ of 345 ng/mL, and an oral $AUC_{0-\infty}$ of 960 ng•h/mL. |
| | **Animal Model:** | Male ob/ob mice[1] |
| | **Dosage:** | Intravenous dose, 5 mg/kg; oral dose, 10 mg/kg |
| | **Administration:** | Intravenous injection and oral gavage; Intravenous dose, 5 mg/kg; oral dose, 10 mg/kg; once |
| | **Result:** | Showed a plasma half-life of 1.1 h, a bioavailability of 50%, a $Cl_p$ of 54 ml/min/kg, an oral $T_{max}$ of 0.25 h, an oral $C_{max}$ of 2177 ng/mL, and an oral $AUC_{0-\infty}$ of 3068 ng•h/mL. |
| | **Animal Model:** | Twenty male Sprague-Dawley rats (350-400 g) fasted and then refed a high sucrose diet for 2 days; additional eight rats fasted for 24 h[1] |
| | **Dosage:** | 100 mg/kg |
| | **Administration:** | Oral gavage; 100 mg/kg; once |
| | **Result:** | Resulted in time-dependent reductions in RQ (a ratio of $CO_2$ production to $O_2$ consumption) of up to 64%. |

**Solvent&Solubility**

**细胞实验:**

DMSO 中的溶解度 ：100 mg/mL (205.92 mM; 超声助溶; 吸湿的 DMSO 对产品的溶解度有显著影响，请使用新开封的 DMSO)

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.0592 mL | 10.2961 mL | 20.5922 mL |
| | 5 mM | 0.4118 mL | 2.0592 mL | 4.1184 mL |
| | 10 mM | 0.2059 mL | 1.0296 mL | 2.0592 mL |

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

**动物实验：**

请根据您的 实验动物和给药方式 选择适当的溶解方案。

以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用；

以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

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|---|---|
| | 方案 一<br>请依序添加每种溶剂： 10% DMSO → 40% PEG300 → 5% Tween-80 → 45% Saline<br>Solubility: ≥ 2.5 mg/mL (5.15 mM); 澄清溶液<br>此方案可获得 ≥ 2.5 mg/mL（饱和度未知）的澄清溶液。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；再向上述体系中加入 50 μL Tween-80，混合均匀；然后再继续加入 450 μL 生理盐水 定容至 1 mL。<br>生理盐水的配制：将 0.9 g 氯化钠，溶解于 ddH₂O 并定容至 100 mL，可以得到澄清透明的生理盐水溶液。<br>方案 二<br>请依序添加每种溶剂： 10% DMSO → 90% (20% SBE-β-CD in Saline)<br>Solubility: ≥ 2.5 mg/mL (5.15 mM); 澄清溶液<br>此方案可获得 ≥ 2.5 mg/mL（饱和度未知）的澄清溶液。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液 中，混合均匀。<br>2 g SBE-β-CD（磺丁基醚 β-环糊精）粉末定容于 10 mL 的生理盐水中，完全溶解至澄清透明。<br>方案 三<br>请依序添加每种溶剂： 10% DMSO → 90% Corn Oil<br>Solubility: ≥ 2.5 mg/mL (5.15 mM); 澄清溶液<br>此方案可获得 ≥ 2.5 mg/mL（饱和度未知）的澄清溶液，此方案实验周期在半个月以上的动物实验酌情使用。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。 |
| **参考文献** | [1]. Harwood HJ Jr, et al. Isozyme-nonselective N-substituted bipiperidylcarboxamide acetyl-CoA carboxylase inhibitors reduce tissue malonyl-CoA concentrations, inhibit fatty acid synthesis, and increase fatty acid oxidation in cultured cells and in experiment<br>[2]. Yamashita T, et al. Design, synthesis, and structure-activity relationships of spirolactones bearing 2-ureidobenzothiophene as acetyl-CoA carboxylases inhibitors. Bioorg Med Chem Lett. 2011 Nov 1;21(21):6314-8.<br>[3]. Daniel Hess, et al. Inhibition of stearoylCoA desaturase activity blocks cell cycle progression and induces programmed cell death in lung cancer cells. PLoS One. 2010 Jun 30;5(6):e11394. |

## 完整储备液配制表：

请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80° C, 6 months; -20° C, 1 month。-80° C 储存时，请在 6 个月内使用，-20° C 储存时，请在 1 个月内使用。

| 可选溶剂 | 质量 / 溶剂体积 / 浓度 | 1 mg | 5 mg | 10 mg | 25 mg |
|---|---|---|---|---|---|
| DMSO | 1 mM | 2.0592 mL | 10.2961 mL | 20.5922 mL | 51.4806 mL |
| | 5 mM | 0.4118 mL | 2.0592 mL | 4.1184 mL | 10.2961 mL |

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|---|---|---|---|---|---|
| | **10 mM** | 0.2059 mL | 1.0296 mL | 2.0592 mL | 5.1481 mL |
| | **15 mM** | 0.1373 mL | 0.6864 mL | 1.3728 mL | 3.4320 mL |
| | **20 mM** | 0.1030 mL | 0.5148 mL | 1.0296 mL | 2.5740 mL |
| | **25 mM** | 0.0824 mL | 0.4118 mL | 0.8237 mL | 2.0592 mL |
| | **30 mM** | 0.0686 mL | 0.3432 mL | 0.6864 mL | 1.7160 mL |
| | **40 mM** | 0.0515 mL | 0.2574 mL | 0.5148 mL | 1.2870 mL |
| | **50 mM** | 0.0412 mL | 0.2059 mL | 0.4118 mL | 1.0296 mL |
| | **60 mM** | 0.0343 mL | 0.1716 mL | 0.3432 mL | 0.8580 mL |
| | **80 mM** | 0.0257 mL | 0.1287 mL | 0.2574 mL | 0.6435 mL |
| | **100 mM** | 0.0206 mL | 0.1030 mL | 0.2059 mL | 0.5148 mL |