

Product Data Sheet

Product Name: 4-CPPC
Cat. No.: GC46630

Chemical Properties

Cas. No. 29553-70-6

SMILES OC(C1=NC=C(C(O)=O)C(C2=CC=CC(C(O)=O)=C2)=C1)=O

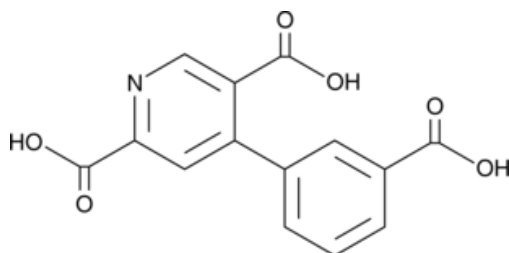
Formula C₁₄H₉NO₆ M.Wt 287.2

Solubility DMSO : 100 mg/mL (348.17 mM; Need ultrasonic) 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

Cell experiment [1]:

Cell lines PBMC-derived macrophages

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

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Preparation Method Macrophages were cultured in the full RPMI 1640 medium at 37°C, and then changed to MEM medium containing 0.2% BSA for 2-4h to achieve starvation. Later, cells were pre-incubated with inhibitors (10μM AMD3100, 4-IPP, or 4-CPPC) for 30min along with 1μg/mL MIF-2 overnight. The second day, cells were cultured in the same medium added with 1% 2-hydroxypropyl-β-cyclodextrin (HPCD) at 37°C for 45min. After rinsing with PBS three times, macrophages were maintained in 25μg/mL Dil-LDL solution at 4°C for 30min and subsequently moved to 37°C for 20min. Measure cellular uptake of Dil-LDL.

Reaction Conditions 10μM; overnight

Applications 4-CPPC inhibits MIF-2-induced enhancement of LDL uptake in cells.

Animal experiment [1]:

Animal models Male *Apoe*^{-/-} mice (C57BL/6)

Preparation Method Eight-week-old male *Apoe*^{-/-} mice were randomly divided into two groups of 11 mice each. The experimental group was administered with 100μg of 4-CPPC dissolved in physiological saline (0.9% NaCl) intraperitoneally every other day for 4.5 weeks; while the control group received saline at the same time intervals.

Dosage form 5mg/kg; i.p.

Applications Atherosclerotic lesion size in aortic root was markedly decreased in 4-CPPC-treated mice compared with controls. Similarly, there was a reduction in lesional macrophages and circulating cytokines and chemokines, such as IL-1α, IL-6, IL-15, and IFN-γ

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References:

[1] El Bounkari O, Zan C, Yang B, et al. An atypical atherogenic chemokine that promotes advanced atherosclerosis and hepatic lipogenesis. *Nat Commun.* 2025;16(1):2297.

Background

4-CPPC is a reversible, selective small molecule inhibitor of the pro-inflammatory protein macrophage migration inhibitor-2 (MIF-2), with K_i values of 431 ± 37 and $33 \pm 0.7 \mu\text{M}$ for MIF-1 and MIF-2, respectively^[1]. 4-CPPC inhibits MIF-1 by specifically binding to its C-terminal region and inducing conformational changes^[1].

In vitro, pre-treatment with $10 \mu\text{M}$ 4-CPPC for 30min, followed by overnight incubation with $1 \mu\text{g/mL}$ MIF-2, attenuated Low-Density Lipoprotein (LDL) uptake in PBMC-derived macrophages^[2]. Treatment of primary astrocytes with $100 \mu\text{M}$ 4-CPPC for 24h attenuated MIF-2 ($1 \mu\text{g/mL}$)-induced activation of the COX-2/PGE2 (Cyclooxygenase-2/Prostaglandin E2) pathway^[3].

In vivo, intraperitoneal administration of 4-CPPC (5mg/kg, every other day over 4.5 weeks) markedly reduced aortic root lesion size, along with lesional macrophages and circulating cytokines/chemokines (e.g., IL-1 α , IL-6, IL-15, and IFN- γ) in Apolipoprotein E knockout (*Apoe*^{-/-}) mice^[2]. In a rat spinal cord injury (SCI) model, intrathecal injection of $8 \mu\text{L}$ 100mM 4-CPPC at the lesion site increased BBB (Basso, Beattie, and Bresnahan) scores within 21 days, significantly improving hindlimb motor recovery^[3].

References:

[1] Pantouris G, Bucala R, Lolis EJ. Structural Plasticity in the C-Terminal Region of Macrophage Migration Inhibitory Factor-2 Is Associated with an Induced Fit Mechanism for a Selective Inhibitor. *Biochemistry.* 2018;57(26):3599-3605.

[2] El Bounkari O, Zan C, Yang B, et al. An atypical atherogenic chemokine that promotes advanced atherosclerosis and hepatic lipogenesis. *Nat Commun.* 2025;16(1):2297.

[3] Ji H, Zhang Y, Chen C, et al. D-dopachrome tautomerase activates COX2/PGE2 pathway of astrocytes to mediate inflammation following spinal cord injury. *J Neuroinflammation.* 2021;18(1):130.

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