

Product Data Sheet

Product Name: MCC950 sodium

Cat. No.: GC10634

Chemical Properties

Cas. No. 256373-96-3

Chemical Name sodium ((1,2,3,5,6,7-hexahydro-s-indacen-4-yl)carbamoyl)((4-(2-hydroxypropan-2-yl)furan-2-yl)sulfonyl)amide

SMILES O=C(NC1=C2CCCC2=CC3=C1CCC3)[N-]S(=O)(C4=CC(C(O)(C)C)=CO4)=O.[Na+]

Formula $C_{20}H_{23}N_2NaO_5S$ M.Wt 426.5

Solubility ≥ 21.45 mg/mL in DMSO, ≥ 100 mg/mL in Water with gentle warming, ≥ 43 mg/mL in EtOH Storage Store at $-20^{\circ}C$

General tips For obtaining a higher solubility, please warm the tube at $37^{\circ}C$ and shake it in the ultrasonic bath for a while. Stock solution can be stored below $-20^{\circ}C$ for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

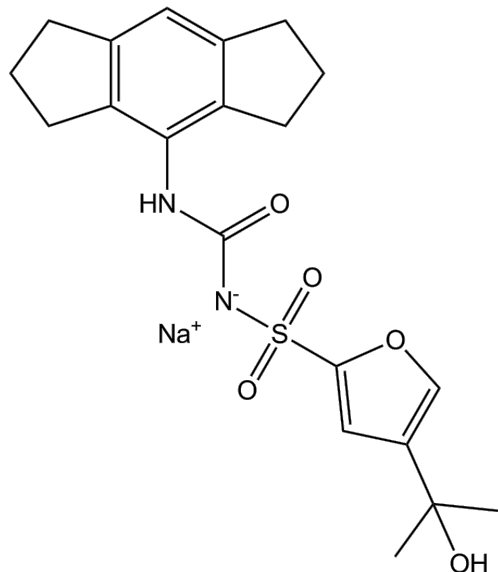
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

Cell experiment [1]:	
Cell lines	H9c2 cells (rat embryonic ventricular cardiomyocyte line)
Preparation Method	H9c2 cells were cultured in DMEM with 10% FBS at 37°C, 5% CO ₂ . Cells were pretreated with MCC950 sodium at 7.5nM for 1 hour, followed by 1μM doxorubicin treatment for 24 hours. After treatment, cell viability (CCK-8), LDH release, ATP content, ELISA for IL-1β and IL-18, immunofluorescence for NLRP3 and caspase-1, qPCR and Western blot for NLRP3/ASC/caspase-1/GSDMD/IL-1β/IL-18 cleavage were assessed.

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Reaction Conditions	7.5nM; 1h pretreatment
Applications	MCC950 sodium increased H9c2 cell viability and improved cell morphology, inhibited LDH release, increased ATP content, decreased IL-1 β and IL-18 levels, reduced NLRP3 and caspase-1 fluorescence signals, and attenuated doxorubicin-induced cleavage of NLRP3, ASC, caspase-1, GSDMD, IL-1 β and IL-18 at protein and mRNA levels.
Animal experiment [2]:	
Animal models	apoE ^{-/-} mice
Preparation Method	Mice were fed a high-fat diet (0.15% cholesterol+21% fat) for 12 weeks and intraperitoneally injected with MCC950 sodium at 10mg/kg three times a week for 12 weeks concurrently with the high-fat diet. After 6 weeks, complete aortas of two mice per group were stained by en face Oil red O; after 12 weeks, venous blood, heart and whole aortic tree were harvested for serum analysis, en face Oil red O staining, aortic root HE/Oil red O/immunofluorescence/TUNEL staining, RT-qPCR and Western blot.
Dosage form	10mg/kg; i.p.; three times a week for 12 weeks

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Applications	MCC950 sodium reduced plaque areas of whole aortas and aortic root, lowered plaque lipid contents, decreased aortic macrophage content and intra-macrophage NLRP3 expression, inhibited ASC oligomerization and protein expressions of NLRP3 and Caspase-1 in aorta, reduced aortic IL-1 β , IL-18 and GSDMD-N protein levels and GSDMD-N fluorescence in macrophages, lowered TUNEL-positive cells in aortic root, and reduced serum TNF- α , IL-1 β , IL-6 and IL-18 levels, without changing serum TG, TC, LDL-C, HDL-C, ox-LDL levels, body weight, or liver/kidney/bone marrow toxicity.
References: [1] Zhang L, Jiang Y, Fan C, et al. MCC950 attenuates doxorubicin-induced myocardial injury in vivo and in vitro by inhibiting NLRP3-mediated pyroptosis. <i>Biomedicine & Pharmacotherapy</i>. 2021 Nov;143:112133. [2] Zeng W, Wu D, Sun Y, et al. The selective NLRP3 inhibitor MCC950 hinders atherosclerosis development by attenuating inflammation and pyroptosis in macrophages. <i>Scientific Reports</i>. 2021 Sep 29;11:19305.	

Background

MCC950 sodium is a novel, orally active NLRP3 inflammasome inhibitor (IC₅₀=7.5nM-8.1nM). MCC950 sodium binds to the NACHT domain of NLRP3 and blocks ATP hydrolysis to inhibit NLRP3 inflammasome activation, reducing the release of pro-inflammatory cytokines such as IL-1 β and IL-18. MCC950 sodium can be used in research related to inflammatory diseases, cardiovascular diseases, and neurodegenerative diseases^[1-4].

In vitro, H9c2 cells were pretreated with 7.5nM MCC950 sodium for 1 hour and then treated with 1 μ M doxorubicin for 24 hours. MCC950 sodium inhibited the cleavage of NLRP3, caspase-1, ASC, GSDMD, IL-1 β and IL-18 in myocardium, improved cell viability and morphology, and suppressed NLRP3-mediated pyroptosis^[5]. PC12 cells were pretreated with 10 μ M MCC950 sodium for 2 hours. MCC950 sodium inhibited oxygen-glucose deprivation/reoxygenation-induced reactive oxygen species production, maintained mitochondrial membrane potential, and reduced pyroptosis and

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nuclear pyknosis in PC12 cells^[6]. THP-1 cells induced by SARS-CoV-2 were treated with MCC950 sodium. MCC950 sodium inhibited IL-1 β secretion and IL-6 production, and suppressed ASC oligomerization promoted by SARS-CoV-2 N protein^[7].

In vivo, apoE^{-/-} mice on a high-fat diet were intraperitoneally injected with 10mg/kg MCC950 sodium three times per week for 12 weeks. MCC950 sodium reduced aortic plaque area and macrophage content, and inhibited NLRP3 and Caspase-1 protein expression and ASC oligomerization in the aorta^[8]. foz/foz mice were orally gavaged with 20mg/kg MCC950 sodium five days per week for 9 weeks. MCC950 sodium decreased plasma ALT and AST levels, reduced plasma IL-1 β , MCP-1 and IL-6 levels, and decreased hepatic NLRP3, active caspase-1 and IL-1 β protein expression^[9]. LPS-induced C57BL/6 mice were prophylactically intraperitoneally injected with 50mg/kg MCC950 sodium. MCC950 sodium reduced serum IL-1 β and IL-6 concentrations^[10].

References:

- [1] Li H, Guan Y, Liang B, et al. Therapeutic potential of MCC950, a specific inhibitor of NLRP3 inflammasome. Eur J Pharmacol. 2022 Aug 5;928:175091.
- [2] Coll RC, Hill JR, Day CJ, et al. MCC950 directly targets the NLRP3 ATP-hydrolysis motif for inflammasome inhibition. Nat Chem Biol. 2019 Jun;15(6):556-559.
- [3] Bakhshi S, Shamsi S. MCC950 in the treatment of NLRP3-mediated inflammatory diseases: Latest evidence and therapeutic outcomes. Int Immunopharmacol. 2022 May;106:108595.
- [4] Zheng Y, Zhang X, Wang Z, et al. MCC950 as a promising candidate for blocking NLRP3 inflammasome activation: A review of preclinical research and future directions. Arch Pharm (Weinheim). 2024 Nov;357(11):e2400459.
- [5] Zhang L, Jiang YH, Fan C, et al. MCC950 attenuates doxorubicin-induced myocardial injury in vivo and in vitro by inhibiting NLRP3-mediated pyroptosis. Biomedicine & Pharmacotherapy. 2021 Nov;143:112133.
- [6] Wang Y, Yuan H, Shen D, et al. Artemisinin attenuated ischemic stroke induced pyroptosis by inhibiting ROS/TXNIP/NLRP3/Caspase-1 signaling pathway. Biomedicine & Pharmacotherapy. 2024 Aug;177:116894.

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- [7] Pan P, Shen M, Yu Z, et al. SARS-CoV-2 N protein promotes NLRP3 inflammasome activation to induce hyperinflammation. *Nature Communications*. 2021 Aug 2;12:4664.
- [8] Zeng W, Wu D, Sun Y, et al. The selective NLRP3 inhibitor MCC950 hinders atherosclerosis development by attenuating inflammation and pyroptosis in macrophages. *Scientific Reports*. 2021 Sep 29;11:19305.
- [9] Mridha AR, Wree A, Robertson AAB, et al. NLRP3 inflammasome blockade reduces liver inflammation and fibrosis in experimental NASH in mice. *Journal of Hepatology*. 2017 May;66(5):1037-46.
- [10] Coll RC, Robertson AAB, Chae JJ, et al. A small molecule inhibition of the NLRP3 inflammasome is a potential therapeutic for inflammatory diseases. *Nature Medicine*. 2015 Mar;21(3):248-55.

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