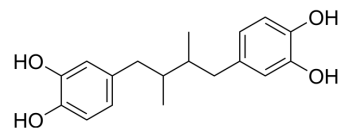


Nordihydroguaiaretic acid

Cat. No.:	HY-N0198												
CAS No.:	500-38-9												
Molecular Formula:	C ₁₈ H ₂₂ O ₄												
Molecular Weight:	302.36												
Target:	Lipoxygenase; Autophagy; Ferroptosis												
Pathway:	Metabolic Enzyme/Protease; Autophagy; Apoptosis												
Storage:	<table border="0"> <tr> <td>Powder</td> <td>-20°C</td> <td>3 years</td> </tr> <tr> <td></td> <td>4°C</td> <td>2 years</td> </tr> <tr> <td>In solvent</td> <td>-80°C</td> <td>6 months</td> </tr> <tr> <td></td> <td>-20°C</td> <td>1 month</td> </tr> </table>	Powder	-20°C	3 years		4°C	2 years	In solvent	-80°C	6 months		-20°C	1 month
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	-20°C	1 month											



SOLVENT & SOLUBILITY

In Vitro	DMSO : 250 mg/mL (826.83 mM; Need ultrasonic)																			
	<table border="1"> <thead> <tr> <th rowspan="2">Concentration</th> <th colspan="3">Mass</th> </tr> <tr> <th>1 mg</th> <th>5 mg</th> <th>10 mg</th> </tr> </thead> <tbody> <tr> <td>1 mM</td> <td>3.3073 mL</td> <td>16.5366 mL</td> <td>33.0732 mL</td> </tr> <tr> <td>5 mM</td> <td>0.6615 mL</td> <td>3.3073 mL</td> <td>6.6146 mL</td> </tr> <tr> <td>10 mM</td> <td>0.3307 mL</td> <td>1.6537 mL</td> <td>3.3073 mL</td> </tr> </tbody> </table>	Concentration	Mass			1 mg	5 mg	10 mg	1 mM	3.3073 mL	16.5366 mL	33.0732 mL	5 mM	0.6615 mL	3.3073 mL	6.6146 mL	10 mM	0.3307 mL	1.6537 mL	3.3073 mL
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Please refer to the solubility information to select the appropriate solvent.																				
In Vivo	<ol style="list-style-type: none"> Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.08 mg/mL (6.88 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.08 mg/mL (6.88 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.08 mg/mL (6.88 mM); Clear solution 																			

BIOLOGICAL ACTIVITY

Description	Nordihydroguaiaretic acid is a 5-lipoxygenase (5LOX) (IC ₅₀ =8 μM) and tyrosine kinase inhibitor.
IC₅₀ & Target	5-LOX 8 μM (IC ₅₀)
In Vitro	The natural dicatechol Nordihydroguaiaretic acid (NDGA) is a selective 5LOX inhibitor from the creosote plant (<i>Larrea tridentata</i> ; Zygophyllaceae). The 5LOX-inhibiting natural dicatechol Nordihydroguaiaretic acid is a very effective, non-toxic

antagonist of TNF α -stimulated microglial activation. Nordihydroguaiaretic acid is approximately six times more potent than Minocycline in vitro, with an IC₅₀ value of 8 \pm 3 μ M and no toxicity at 100 μ M. Significant NO₂⁻ suppression is observed at 800 nM Nordihydroguaiaretic acid. Similar efficacy is observed for natural and synthetic Nordihydroguaiaretic acid, as well as for the acetyl ester of Nordihydroguaiaretic acid. Nordihydroguaiaretic acid also suppresses TNF α -stimulated PGE₂ production by EOC-20 cells with an IC₅₀ of 841 nM^[1]. To test the proliferation effect of prostaglandin E1 and Nordihydroguaiaretic acid (NDGA) on cancer cell lines, HepG2 cell lines are treated with various doses of the two compounds and the positive compounds 8-anilino-1-naphtalene sulfonate (ANS), respectively, for 24 h and cell viability is examined by the MTT assay. ANS displays a dose-dependent inhibition (0, 10, 30, 50, 80, 100, 120, and 150 μ M) with the estimated IC₅₀ being 25.888 μ M. The tested IC₅₀ of prostaglandin E1 is 41.223 μ M and Nordihydroguaiaretic acid is 45.646 μ M, respectively, at different concentrations of 0, 30, 60, 80, 100, 120, and 140 μ M^[2].

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

In Vivo

Compared with the control ob/ob chow diet group, there is a significant reduction of body weight starting from 9 wk treatment in the high-dose Nordihydroguaiaretic acid (NDGA) diet group, and from 12 wk in the low-dose group. Nordihydroguaiaretic acid treatment results in higher body (rectal) temperatures of ob/ob mice, especially with the high dose of Nordihydroguaiaretic acid^[3].

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

PROTOCOL

Cell Assay^[2]

MTT assay is used to measure cell growth-inhibitory activity of the selected most promising compounds in HepG2 cell lines. Cells are cultured in 96-well culture plate at 1 \times 10⁴ cells/well. After 24 h cultured at 37 °C in the atmosphere of 5% CO₂, cells are adhered and treated with different concentrations of the targeted compounds (e.g., Nordihydroguaiaretic acid, 0, 30, 60, 80, 100, 120, and 140 μ M) and incubated for 24 h. Then, the supernatants are discarded and MTT (0.5 mg/mL) is added to each well and incubated at 37°C in 5% CO₂ for an additional 4 h. Following, the MTT is removed and 150 μ L of formazan in DMSO is added to terminate response and then plates are set to the table shaker for 5 min at low speed. Cell proliferation is evaluated by measuring the absorbance at 570 nm using ELISA Plate Reader. The IC₅₀ values are calculated by SPSS statistics 17.0^[2].

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Animal Administration^[3]

Mice^[3]

Seven-week-old male control C57BL/6J mice, male leptin-deficient (*ob/ob*) mice, and male *Ppara*-deficient mutant mice (B6.129S4-Pparatm1Gonz/J) are used. These mice are fed a standard chow diet for 1 wk to allow them to acclimatize to a controlled new environment (25 \pm 2°C, 55 \pm 5% relative humidity with a 12-h light-dark cycle). Subsequently, one group of ob/ob mice is switched to a chow diet supplemented with either low- (0.83 g/kg chow diet) or high-dose (2.5 g/kg chow diet) Nordihydroguaiaretic acid and maintained on this diet for 16 wk. The other groups of ob/ob mice and control mice continue to be fed a normal chow diet for 16 wk. In another set of studies, C57BL/6J mice and *Ppara*-deficient mutant mice are fed either a high-fat diet (~60% of total calories come from fat), or the same high-fat diet supplemented with a high dose of Nordihydroguaiaretic acid (2.5 g/kg diet). Food intake and body weights are measured once a week throughout the experiment.

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

CUSTOMER VALIDATION

- Biomed Pharmacother. 2020 Jul;127:110151.
- PLoS Negl Trop Dis. 2019 Aug 20;13(8):e0007681.
- Biochem Biophys Res Commun. 2018 Sep 3;503(1):297-303.

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REFERENCES

- [1]. West M, et al. The arachidonic acid 5-lipoxygenase inhibitor Nordihydroguaiaretic acid inhibits tumor necrosis factor alpha activation of microglia and extends survival of G93A-SOD1 transgenic mice. *J Neurochem.* 2004 Oct;91(1):133-43.
- [2]. Lu F, et al. Virtual Screening for Potential Allosteric Inhibitors of Cyclin-Dependent Kinase 2 from Traditional Chinese Medicine. *Molecules.* 2016 Sep 21;21(9). pii: E1259.
- [3]. Zhang H, et al. Nordihydroguaiaretic acid improves metabolic dysregulation and aberrant hepatic lipid metabolism in mice by both PPAR α -dependent and -independent pathways. *Am J Physiol Gastrointest Liver Physiol.* 2013 Jan 1;304(1):G72-86.
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