L6H21

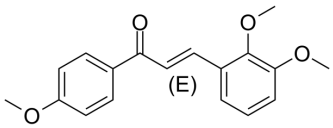
Cat. No.: HY-W082785A

CAS No.: 24533-47-9

Molecular Formula: $C_{18}H_{18}O_4$

Molecular Weight: 298.33

Target: TNF Receptor; Interleukin Related; Toll-like Receptor (TLR); NF-κB; NOD-like Receptor (NLR); Caspase; Apoptosis; Bcl-2 Family; Reactive Oxygen Species



Pathway: Apoptosis; Immunology/Inflammation; NF-κB; Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month

SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (335.20 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.3520 mL	16.7600 mL	33.5199 mL
	5 mM	0.6704 mL	3.3520 mL	6.7040 mL
	10 mM	0.3352 mL	1.6760 mL	3.3520 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (8.38 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (8.38 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

L6H21, a Chalcone (HY-121054) derivative, is an orally active, potent and specific myeloid differentiation 2 (MD-2) inhibitor. L6H21 directly binds to MD-2 protein with a high affinity and low K_D value of 33.3 μM, blocking the formation of the LPS-TLR4/MD-2 complex. L6H21 inhibits LPS-induced expression of TNF-α and IL-6 in RAW264.7 macrophages, with IC_{50} values of 6.58 and 8.59 μM, respectively. L6H21 can be used for alcoholic liver disease, metabolic disturbance and neuroinflammation research[1][2][3].

IC_{50} & Target				
	IL-6 8.59 μM (IC_{50})	TLR4	NF-κB	NLRP3 inflammasome

	IL-1β	Caspase 3	Bcl-2	Bax

In Vitro

L6H21 (10 μM, 2 h) inhibits EtOH + LPS-induced apoptosis and mitochondrial damage in RAW264.7 cells[1].
L6H21 (10 μM, 2 h) attenuates EtOH + LPS-induced ROS formation and TLR4–NF-κB activation, and decreases NLRP3 inflammasome activation[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	RAW264.7 cells (mouse macrophage cell line)
Concentration:	10 μM
Incubation Time:	2 hours
Result:	Markedly decreased apoptotic cell numbers; completely inhibited EtOH + LPS-induced increase in Bax/Bcl-2; markedly decreased EtOH + LPS-induced elevation in cleaved caspase-3 protein.

Western Blot Analysis[1]

Cell Line:	RAW264.7 cells (mouse macrophage cell line)
Concentration:	10 μM
Incubation Time:	2 hours
Result:	Reduced EtOH + LPS-induced TLR4–NF-κB signaling; completely inhibited the increase in TLR4 and NF-κB p65 nuclear level induced by EtOH and LPS. Attenuated EtOH + LPS-induced expression of NLRP3 inflammasome; inhibited the elevated NLRP3 and IL-1β protein expression; decreased the expression of p20, an active form of caspase-1.

Cell Viability Assay[1]

Cell Line:	RAW264.7 cells (mouse macrophage cell line)
Concentration:	10 and 20 μM
Incubation Time:	2 hours
Result:	The loss of cell viability by EtOH + LPS was prevented by L6H21 pretreatment. Slightly decreased cell viability a higher dose of 20 μM.

In Vivo

L6H21 (10 mg/kg, Oral gavage, daily) effectively inhibits EtOH + LPS-induced hepatic fat accumulation, hepatic steatosis and liver injury[1].
L6H21 (0-40 mg/kg, Orally, daily for 4 weeks) attenuates metabolic disturbance, restores cognition and attenuates brain pathologies dose and time-dependently in HFD-fed rats, and shows neuroprotective effect in a model of prediabetes[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male C57BL6 mice (8-10 weeks old, n = 36, 8 mice in each group, 25-30 g, with EtOH and LPS)[1]
Dosage:	10 mg/kg
Administration:	Oral gavage, daily, before EtOH feeding
Result:	Decreased hepatic triglyceride (TG) concentration, markedly decreased serum alanine

	transaminase (ALT) and aspartate transaminase (AST) levels; Significantly decreased inflammation in liver tissue induced by EtOH + LPS.
Animal Model:	Male Wistar rats (6-7 weeks old, 250 g, a normal diet (ND) (n=8) or a high-fat diet (HFD) (n=104) for 16 weeks)[2]
Dosage:	0, 10, 20, and 40 mg/kg
Administration:	Orally, daily for 1, 2 or 4 weeks
Result:	Ameliorated brain mitochondrial dysfunction in HFD-fed rats at 2-week administration time point; improved brain mitochondrial function in a dose-dependent manner for 4 weeks. Reduced hippocampal apoptosis in prediabetes for 4 weeks. Attenuated the reduction of dendritic spine volume and density for 4 weeks. Preserved microglial morphology in a dose-dependent manner.

REFERENCES

[1]. Kong X, et al. Chalcone Derivative L6H21 Reduces EtOH + LPS-Induced Liver Injury Through Inhibition of NLRP3 Inflammasome Activation. Alcohol Clin Exp Res. 2019 Aug;43(8):1662-1671.

[2]. Oo TT, et al. L6H21 protects against cognitive impairment and brain pathologies via toll-like receptor 4-myeloid differentiation factor 2 signalling in prediabetic rats. Br J Pharmacol. 2022 Mar;179(6):1220-1236.

[3]. Yi Wang, et al. MD-2 as the target of a novel small molecule, L6H21, in the attenuation of LPS-induced inflammatory response and sepsis. Br J Pharmacol. 2015 Sep;172(17):4391-405.

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