Product Data Sheet

Product Name: Z-Guggulsterone
Cat. No.: GC10195

Chemical Properties

Cas. No.	39025-23-5		
Chemical Name	(8S,9R,10R,13R,14S,Z)-17-ethylidene-10,13-dimethyl-7,8,9,10,11,12,13,14,15,17-decahydro-1H-cyclopenta[a]phenanthrene-3,16(2H,6H)-dione		
SMILES	O=C1C[C@H]([C@@](/C1=C/C)(C)CC2)[C@@H](CC3)[C@@H]2[C@](CC4)(C)C3=CC4=O		
Formula	$C_{21}H_{28}O_2$	M.Wt	312.45
Solubility	≥ 3.12mg/mL in DMSO with ultrasonic and warming	Storage	Store at RT
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.		

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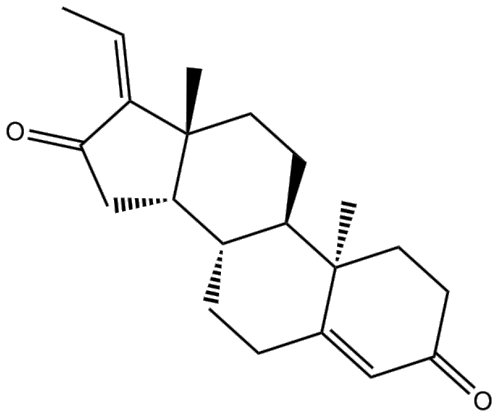
Structure



Protocol

Cell experiment [1]:

Cell lines	Bone marrow-derived macrophage (BMDM)
Preparation Method	Cells were incubated with Z-Guggulsterone at increasing concentrations (0, 0.5, 5, and 20 M) for 1 h and then simulated with LPS in the presence or absence of TREM-1 agonist antibody for the indicated time.
Reaction Conditions	0.5-20uM Z-Guggulsterone for 1h

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Applications	Z-Guggulsterone attenuates TREM-1-mediated hyperactivation of macrophages through inhibition of TREM-1 expression and NF-κB and AP-1 activation.

Animal experiment [2]:

Animal models	IL-10, TLR4, and MyD88 deficient mice
Preparation Method	Z-Guggulsterone were administered orally at 100 mg/kg once daily after TNBS administration for 4 days or throughout the experiment. The mice were monitored for weight loss, fecal consistency, presence of crude blood in the feces or anus, and overall mortality
Dosage form	100 mg/kg Z-Guggulsterone orally administered once daily for 4 days
Applications	Z-Guggulsterone improves colitis in mice by regulating macrophage phenotype through IL-10 and TLR4/MyD88 pathways.

References:

[1]: Che X, Park KC, et,al. Protective effects of guggulsterone against colitis are associated with the suppression of TREM-1 and modulation of macrophages. Am J Physiol Gastrointest Liver Physiol. 2018 Jul 1;315(1):G128-G139. doi: 10.1152/ajpgi.00027.2018. Epub 2018 Mar 15. PMID: 29543509.

Background

Z-Guggulsterone is a steroidal plant active ingredient derived from *Commiphora mukul* and can promote cancer cell apoptosis. Z-Guggulsterone acts as a selective farnesoid X receptor (FXR) antagonist to downregulate ACE2 expression and inhibit SARS-CoV-2 infection. Z-Guggulsterone reduces neuroinflammation by blocking the IκBα-NF-κB signaling pathway. Z-Guggulsterone can be used in research related to hypercholesterolemia, prostate cancer, and COVID-19[1-4].

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In vitro, BV2 microglial cells and mouse primary microglial cells were pretreated with Z-Guggulsterone (30μM) for 30min, and then stimulated with LPS (1μg/ml) for 6–24h. Z-Guggulsterone significantly inhibited the mRNA and protein expression of iNOS, TNF-α, and IL-6, reduced NO production, attenuated LPS-induced IκBα degradation, and blocked NF-κB nuclear translocation[5]. Human gastric cancer SGC-7901 cells and human normal gastric epithelial GES-1 cells were treated with Z-Guggulsterone (15–75μM) for 24h. Z-Guggulsterone inhibited the expression of FXR and SHP in cells, suppressed the proliferation of SGC-7901 cells, promoted apoptosis, upregulated Bax and active caspase-3 expression, downregulated Bcl-2 expression, increased TNF-α content, and decreased VEGF and TGF-β1 content[6].

In vivo, Z-Guggulsterone (30 and 60mg/kg) was intraperitoneally injected into scopolamine-induced memory-impaired C57BL/6J mice for 10 consecutive days (scopolamine 2mg/kg was given 30min after the last administration). Z-Guggulsterone effectively reversed scopolamine-induced memory impairment, restored the step-through latency in passive avoidance test and the spontaneous alternation rate in Y-maze test, shortened the escape latency in Morris water maze and prolonged the swimming time in the target quadrant, inhibited the increase in AChE activity in the hippocampus and cortex, and upregulated BDNF protein expression and the phosphorylation levels of CREB, ERK1/2, and Akt[7]. Z-Guggulsterone (10, 30mg/kg) was intraperitoneally injected once into C57BL/6J mice, and tail suspension test and forced swim test were performed 30min later. Z-Guggulsterone (10, 30mg/kg; once daily; for 12 consecutive days) was intraperitoneally injected into chronic unpredictable stress-induced depression model C57BL/6J mice. Acute administration of Z-Guggulsterone reduced the immobility time in tail suspension test and forced swim test in mice, without affecting locomotor activity. Chronic administration of Z-Guggulsterone reduced the immobility time in tail suspension test and forced swim test in chronic unpredictable stress model mice, increased sucrose intake, upregulated BDNF protein expression in the hippocampus and medial prefrontal cortex, elevated the phosphorylation levels of CREB, ERK1/2, and Akt, increased the number of DCX-positive cells in the hippocampus, and upregulated DCX protein expression to promote hippocampal neurogenesis[8].

References:
[1] Xiao D, Singh SV. z-Guggulsterone, a constituent of Ayurvedic medicinal plant Commiphora mukul, inhibits angiogenesis in vitro and in vivo. Mol Cancer Ther. 2008 Jan;7(1):171-80.
[2] Brevini T, Maes M, Webb GJ, et al. FXR inhibition may protect from SARS-CoV-2 infection by reducing ACE2. Nature. 2023 Mar;615(7950):134-142.

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[3] Shishodia S, Azu N, Rosenzweig JA, et al. Guggulsterone for Chemoprevention of Cancer. Curr Pharm Des. 2016;22(3):294-306.
[4] Yamada T, Sugimoto K. Guggulsterone and Its Role in Chronic Diseases. Adv Exp Med Biol. 2016;929:329-361.
[5] Huang C, Wang J, Lu X, et al. Z-guggulsterone negatively controls microglia-mediated neuroinflammation via blocking IκB-α-NF-κB signals. Neurosci Lett. 2016 Apr 21;619:34-42.
[6] Lv R, Zhu M, Chen K, et al. Z-Guggulsterone Induces Apoptosis in Gastric Cancer Cells through the Intrinsic Mitochondria-Dependent Pathway. ScientificWorldJournal. 2021 Jan 4;2021:3152304.
[7] Chen Z, Huang C, Ding W. Z-Guggulsterone Improves the Scopolamine-Induced Memory Impairments Through Enhancement of the BDNF Signal in C57BL/6J Mice. Neurochem Res. 2016 Dec;41(12):3322-3332.
[8] Liu FG, Hu WF, Wang JL, et al. Effects of a Janus kinase inhibitor, pyridone 6, on airway responses in a murine model of asthma. Biochem Biophys Res Commun. 2011 Jan 7;404(1):261-7.

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